Ch 13
(293/1961)

UDC 547.81:547.913

ACTA POLYTECHNICA SCANDINAVICA

CHEMISTRY INCLUDING METALLURGY SERIES No. 13

A. RYE ALERTSEN

Ageratochromene, a Heterocyclic Compound from the Essential Oil of *Ageratum houstonianum* Mill.

Norwegian Contribution No. 10

OSLO 1961

ACTA POLYTECHNICA SCANDINAVICA

. . . a Scandinavian contribution to international engineering sciences

Published under the auspices of the Scandinavian Council for Applied Research

in *Denmark* by the Danish Academy of Technical Sciences

in *Finland* by the Finnish Academy of Technical Sciences, the Swedish Academy of Engineering Sciences in Finland, and the State Institute for Technical Research

in *Norway* by the Norwegian Academy of Technical Science and the Royal Norwegian Council for Scientific and Industrial Research

in *Sweden* by the Royal Swedish Academy of Engineering Sciences, the Swedish Natural Science Research Council, and the Swedish Technical Research Council

Acta Polytechnica Scandinavica consists of the following sub-series:
Chemistry including Metallurgy Series, Ch
Civil Engineering and Building Construction Series, Ci
Electrical Engineering Series, El
Mathematics and Computing Machinery Series, Ma
Mechanical Engineering Series, Me
Physics including Nucleonics Series, Ph

For subscription to the complete series or to one or more of the sub-series and for purchase of single copies, please write to

ACTA POLYTECHNICA SCANDINAVICA PUBLISHING OFFICE
Box 5073
Stockholm 5 Telephone 67 09 10

This issue is published by
the Royal Norwegian Council for Scientific and Industrial Research
Oslo, Norway

UDC 547.81: 547.913

AGERATOCHROMENE, A HETEROCYCLIC COMPOUND FROM THE ESSENTIAL OIL OF AGERATUM HOUSTONIANUM MILL.

by

Aase Rye Alertsen
Institutt for Organisk Kjemi,
Norges Tekniske Høgskole, Trondheim

This work has been supported by grants from the Norwegian Research Council for Science and the Humanities, Oslo and from the Royal Norwegian Council for Scientific and Industrial Research, Oslo.

ACTA POLYTECHNICA SCANDINAVICA
Chemistry including Metallurgy Series Ch 13
(Acta P. 293, 1961)

CONTENTS

		Page
	Ageratum houstonianum Mill.	1
2.	Previous work on Ageratum	1
3.	Ageratochromene and derivatives	2
4.	Experimental part	12
4.1.	Isolation of ageratochromene	12
4.2.	Ageratochromene	15
4.3.	3:4-Dihydro-ageratochromene	16
4.4.	3:4-Dihydroxy-ageratochromene	16
4.5.	Oxidation of 3:4-dihydroxy-ageratochromene (III) with sodium dichromate	17
4.6.	Oxidation of 3:4-dihydroxy-ageratochromene with lead tetra-acetate	18
4.7.	Oxidation of (V) with potassium permanganate. The monocarboxylic acid	21
4.8.	The dicarboxylic acid	22
5.	Synthetic substances	24
5.1.	Phenoxyacetone	24
5.2.	Phenoxyglycerol	25
5.3.	Phenoxyacetaldehyde	25
5.4.	Hemipinic acid; 3:4-dimethoxy-phthalic acid	25
5.5.	m-Hemipinic acid; 4:5-dimethoxy-phthalic acid	26
5.6.	α-Bromoisovaleric acid	27
5.7.	ββ-Dimethylacrylic acid	27
5.8.	ββ-Dimethylacryl chloride	27
5.9.	5:7-Dihydroxy-2:2-dimethylchromanone	27
5.10.	5:7-Dihydroxy-2:2-dimethylchroman	28
5.11.	5:7-Dimethoxy-2:2-dimethylchroman	28
5.12.	Veratronitrile	29
5.13.	4-Aminoveratrole; 3:4-dimethoxy-aniline	29
5.14.	3:4-Dimethoxy-phenol	29
5.15.	6:7-Dimethoxy-2:2-dimethylchromanone	30
5.16.	6:7-Dimethoxy-2:2-dimethylchroman	33
6.	The infra-red spectra	34
7.	2:2-Dimethyl-chromene derivatives in Nature	42
	Summary	49
	Acknowledgements	50
	References	51
	Ultraviolet spectra	57
	Infra-red spectra	60

1. AGERATUM HOUSTONIANUM MILL.

Ageratum houstonianum Mill. belongs to the family Compositae, the tribe Eupatorieae and the subtribe Ageratinae[1]. Its native habitats are Mexico and Peru[2]. The genus Ageratum has 30 species[1]. In countries in the temperate zone Ageratum houstonianum and A. conyzoides are much used for decorative purposes in parks etc.

In English-speaking countries or in works written in the English language the name for Ageratum is floss-flower or maudlin[3]. The most common name for Ageratum in French-speaking countries is agérate, but the name agératoire can also be found[3]. In German-speaking countries or in works written in German we find many different names: Balsamleberkraut, Bastardhanf, Dürrwurzel, Malvazierkraut and Leberbalsam, the last being the one officially accepted[3]. In Dutch-speaking countries the name is geurkruid[3]. In Danish A. houstonianum is called blåkvast[4] and in Norwegian blåkorg[5].

A synonym for Ageratum houstonianum Mill. is Ageratum mexicanum Sims[5], the latter being more common in literature. This species is not identical with Ageratum mexicanum Sweet, the correct name of which seems to be Ageratum brachystephanum Reg.[6]. Ageratum is derived from the Greek word agêratos, meaning: not growing old, imperishable[7]. The name probably refers to the long flowering period of the plant. Mexicanum means from Mexico[7], and the name houstonianum possibly was given in memory of the English botanist W. Houston (d. 1733) who wrote about the flora of Mexico and the Antilles[7].

2. PREVIOUS WORK ON AGERATUM

Administration of A. conyzoides L. causes contraction of arterial walls, and in French Guiana the plant has been used in popular medicine in the treatment of bleedings from the uterus. The plant was therefore called the woman's flower (herbe á femme, herbe á madame). In 1910 J. Chevalier[8] published his work on an alkaloid found in this plant. The substance had the same physiological actions as the plant itself. The alkaloid was also found in A. mexicanum, but in smaller quantities. This substance is probably the one called ageratin by Wehmer and Hadders[9].

Chevalier also mentioned that A. conyzoides was used by the natives of Réunion, an island in the Indian Ocean west of Madagascar.

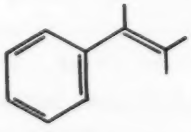
In 1888 H. Molisch and S. Zeisel[10] reported the occurrence of coumarin in A. mexicanum, but they observed that the odour of coumarin was never detected in living plants, only in dead condition.

Moudgill[11] described some of the properties of the essential oil of Appa-grass, A. conyzoides L. The elementary analysis of the major fraction of the oil indicated the composition $C_{12}H_{16}O_2$. Essential oils from certain plants from French Upper Ubangi, French Equatorial Africa, were investigated by L. Joly[12], who found that the oil of A. conyzoides L. consisted almost entirely of a phenolic ester. A trace of free eugenol, but no solid material, was isolated.

3. AGERATOCHROMENE AND DERIVATIVES

The name ageratochromene is proposed for a substance present in the plant Ageratum houstonianum Mill.

When A. houstonianum was distilled with steam, a yellow oil was obtained from which ageratochromene separated by crystallization at -15°C. The white crystals melted at 47.5° and had an elementary composition of $C_{13}H_{16}O_3$ (I). Ageratochromene was optically inactive. On catalytic hydrogenation the hydrogen consumed corresponded to one double bond, and a dihydrocompound $C_{13}H_{18}O_3$ (II) was produced. The two substances had maxima in the ultraviolet at: (I) λ 2800, 3230 Å ($\varepsilon_{max.}$ 5500 and 9200, respectively) Figure I, and (II) λ 2930 Å ($\varepsilon_{max.}$ 6400) Figure 2. The ultraviolet spectra indicated the presence in (I) of a benzene nucleus conjugated with one double bond.



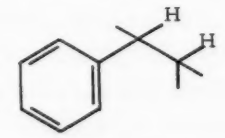
$C_{13}H_{16}O_3$ I

The infra-red spectrum also revealed the aromatic character of (I). The spectra of this compound and all its derivatives had two bands in the regions 1635-1590 cm^{-1} and 1520-1498 cm^{-1}. It could be concluded from the infra-red spectrum of (I) that the substance had no carbonyl or hydroxyl

functions, as there were no maxima in the regions of 1800 - 1650 cm^{-1} and 3700 - 3200 cm^{-1} (Figure 7).

The CH_3-band of the infra-red spectrum was split into two separate maxima at 1362 and 1383 cm^{-1}, the intensity of the first being greater than that of the latter. This is characteristic of the tertiary butyl grouping $(CH_3)_3C$-. With the isopropyl grouping $(CH_3)_2CH$- or $(CH_3)_2$-CR-, resonance splitting also occurs, the two bands having approximately equal intensities. But the intensity pattern may be influenced by the presence of other methyl groups elsewhere in the molecule, which will contribute their own specific absorptions in this region.

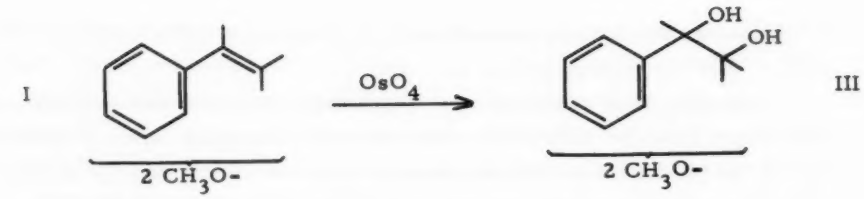
A methoxyl determination of (II) indicated that the substance contained two methoxyl groups. The dihydrocompound (II), $C_{13}H_{18}O_3$, could be written $C_nH_{2n-8}O_3$. Therefore it could be concluded that (II) contained two rings. Since the third oxygen was inert, the possibility further existed that it was contained in a cyclic ether connected with the benzene ring.



$C_{13}H_{18}O_3$ II

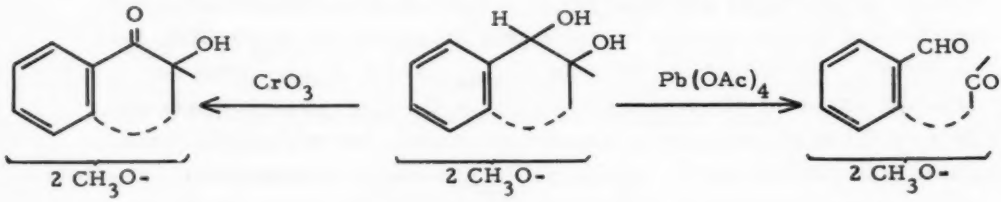
2 CH_3O-

Attempts were made to degrade ageratochromene by oxidation to a substance with a smaller number of C-atoms. Ageratochromene was not attacked by potassium permanganate in acetone at room temperature. But oxidation of (I) with osmium tetroxide gave the glycol, $C_{13}H_{18}O_5$ (III), m. p. 129.5°. The ultraviolet spectrum ($\lambda_{max.}$ 2925 Å, $\varepsilon_{max.}$ 4300) resembled that of the dihydrocompound (Figure 2). The infra-red spectrum (Figure 9) had no maximum in the carbonyl region, but two hydroxyl maxima at 3480 and 3590 cm^{-1}. The glycol (III) formed an acetate (VIII). The methoxyl determination of (VIII) indicated that only one acetyl group had been introduced into the glycol, and this was confirmed by the infra-red spectrum (Figure 10) which had a weak maximum at 3550 cm^{-1} indicating the presence of a hydroxyl group.



Oxidation of (III) with chromic acid produced the compound $C_{13}H_{16}O_5$ (IV) melting at 118.8 - 120° and with ultraviolet absorption maxima at λ 2420, 2745, 3375 and 3485 Å ($\varepsilon_{max.}$ 55200, 13500, 7600 and 6500, respectively), Figure 3. The infra-red spectrum supplied the information that (IV) had a carbonyl group conjugated with a benzene ring (1682 cm^{-1}) and a hydroxyl group (3530 cm^{-1}) (Figure 11).

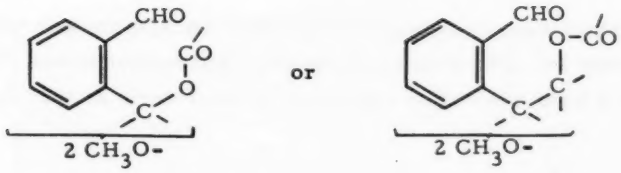
Oxidation of the glycol (III) with lead tetra-acetate gave the substance $C_{13}H_{16}O_5$ (V), with m.p. 101.5 - 102° and ultraviolet absorption maxima at λ 2730 and 3160 Å ($\varepsilon_{max.}$ 15200 and 7700, respectively) Figure 4. According to the infrared spectrum (V) also had a carbonyl group conjugated with the benzene ring (1676 cm^{-1}) (Figure 12). The ultraviolet spectra of (IV) and (V) made it probable that a heterocyclic ring of ageratochromene had not been opened by the oxidation of the glycol with chromic acid. D. Biquard[13] found that a carbonyl group conjugated with a benzene nucleus moves the ultraviolet maximum towards longer wavelengths when the C=O is placed in a sixmembered ring. Since (IV) has a carbonyl group conjugated to the benzene ring, this C-atom has to be substituted with hydrogen.



IV III V

(V) formed a 2:4-dinitrophenylhydrazone with m.p. 213 - 216° and the UV-absorption maximum at 3980 Å.

The infra-red spectrum of (V) also showed a strong peak at 1742 cm^{-1} indicating another carbonyl function. This maximum coincides with the standard value for an isolated ester group. To account for this ester group (V) was proposed to have the formula:

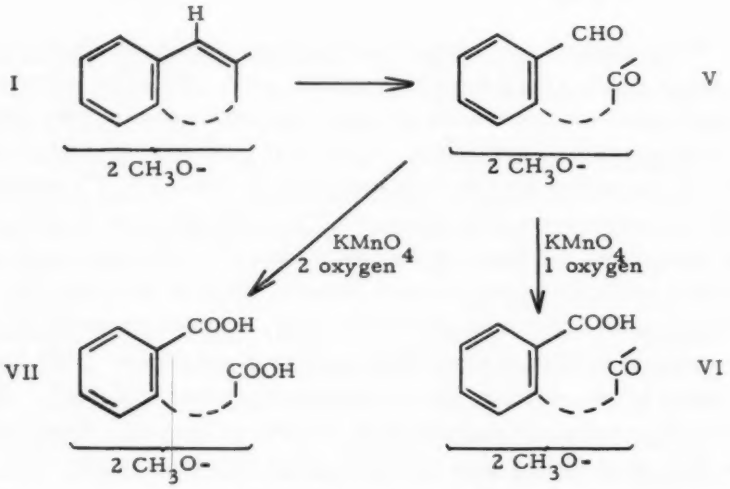


When submitted to further oxidative degradation the first of these structures should give a dimethoxyphthalic acid. When the oxidation was performed with an amount of potassium permanganate corresponding to 3 gramatoms of O_2 per mole of (V), an acid (VII) was obtained in very low yield. A few milligrams of a substance (m.p. 175 - 176.3°) sparingly soluble in choloroform also separated. The melting point of (VII) showed great variations, the limits being 154.5 and 165°. When the melt was allowed to cool, nice crystals were formed, their m.p. being 172 - 174°. Hemipinic acid, 3:4-dimethoxyphthalic acid, exhibits the same peculiarity, owing to formation of various amounts of anhydride. This formation starts before melting, and is considerable already at 140°. The melting point therefore depends upon the time of heating. Wegscheider[14] found that rapid heating gave a melting point between 175 and 179°, whilst on slow heating, with consequent formation of a large portion of anhydride, the m.p. 160 - 162° was observed. Hemipinic acid and (VII) did not give any melting point depression when mixed, and both of them gave the same reddish brown colour with ferric chloride in water. The acid (VII) dissolved readily in chloroform, and the infra-red spectrum was obtained; but hemipinic acid could not be dissolved, even if the water of crystallisation had been removed by sublimation in a high vacuum. The infra-red spectrum of hemipinic acid in a potassium bromide disc (Figure 19) was different from that of (VII) Figure 15.

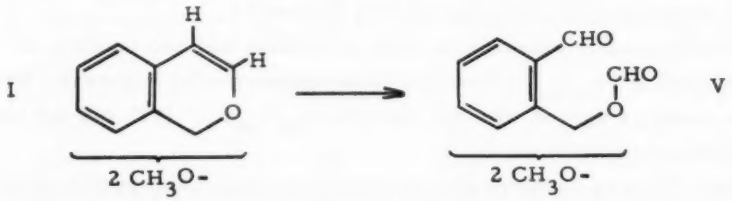
The ultraviolet spectrum of (VII) in ethanol had two maxima at 2570 and 2990 Å ($\varepsilon_{max.}$ 13000 and 7100, respectively) Figure 5. Elementary analysis agreed with the formula $C_{13}H_{16}O_7$. (VII) did not form a 2:4-dinitrophenylhydrazone.

When (V) was oxidized with an amount of potassium permanganate corresponding to one gram atom of oxygen per mole, a monocarboxylic acid $C_{13}H_{16}O_6$ (VI) was obtained with m.p. 118 - 119°, $\lambda_{max.}$ (in ethanol) 2745 and 3320 Å ($\varepsilon_{max.}$ 8500 and 5400, respectively) Figure 5. The infrared spectrum (in a potassium bromide disc) showed bands at

1740 cm^{-1} (normal saturated ester) and at 1640, 1675, 2530 and 2630 cm^{-1} (aryl acid) Figure 14. (VI) Formed a 2:4-dinitrophenylhydrazone with m.p. 210 - 212° and a light absorption maximum in chloroform at 4020 Å ($\varepsilon_{max.}$ 28350).

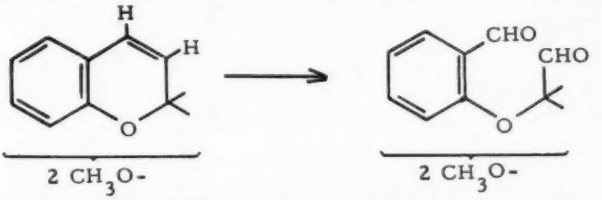


As a mono- and a dicarboxylic acid with the same number of C-atoms, which also is the number of carbon atoms of the parent compound, were obtained, the double bond conjugated with the benzene ring in (I) had to be of the type -CH=CH-. It then became necessary to abandon the theory that the 1740 cm^{-1} band of (V) and (VI) represented a normal saturated ester group, which, being a formate, should have shown a carbonyl frequency in the range 1724- 1722 cm^{-1} [15].



Control measurements of phenoxyacetone, C_6H_5-O-CH_2-CO-CH_3, gave an infra-red maximum at 1735 cm^{-1}. For phenoxyacetaldehyde, C_6H_5-O-CH_2-CHO, the maximum was shifted to 1745 cm^{-1}. This indicated that the 1742 cm^{-1} band of (V) might belong to an isolated aldehyde

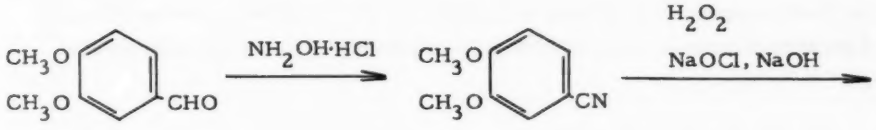
group and that is was displaced from its ordinary position at 1730 - 1675 cm^{-1} by the presence of an α-phenoxy-residue (compare p. 40).

I  V

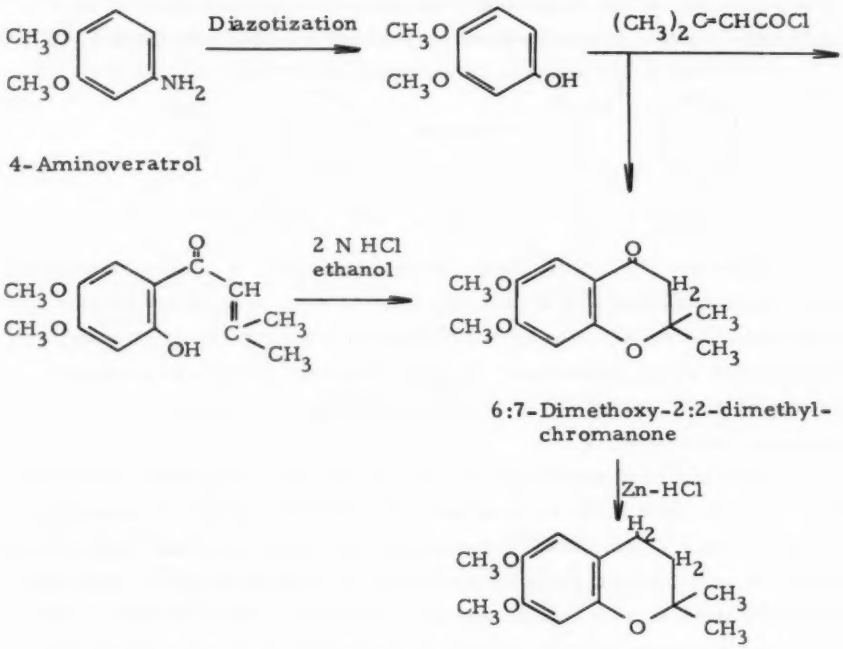
2 CH_3O- 2 CH_3O-

Since the glycol (III) gave a monoketone (IV), a monoacetate (VIII) and a monocarboxylic acid (VI), the carbon atom next to the double bond would be expected to be substituted in a manner as to give an appreciable steric hindrance. A gem. dimethyl group was probable (compare p. 3),and (I) might be assumed to be a dimethoxy-2:2-dimethyl-chromene.

The infra-red spectra of (I) and its derivatives further indicated a 1: 2: 3: 5- or a 1: 2: 4: 5-substituted benzene compound (compare p. 38). The 5:7-dimethoxy-2:2-dimethyl-chroman (IX) was synthesized following a procedure given by Alexander Robertson et al.[16]. (IX) was stated by them to be a liquid, and our synthesis confirmed this. The infra-red spectrum of (IX) showed many similarities with that of (II), but they were not identical (Figures 23 and 8). 6:7-Dimethoxy-2:2-dimethyl-chroman (X) was then synthesized following an analogous procedure, via 3:4-dimethoxy-phenol and $\beta\beta$-dimethyl-acryl chloride.

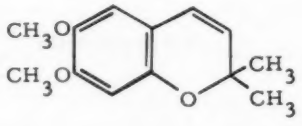


Veratraldehyde Veratronitrile



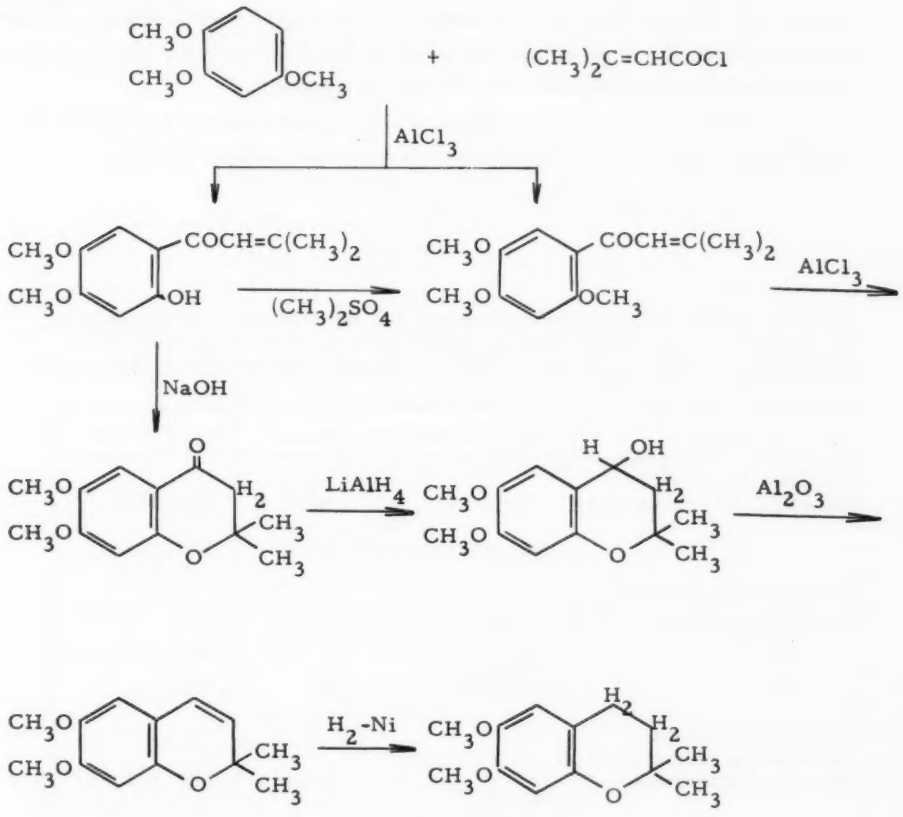
X

(X) turned out to be identical with (II) according to m.p. (58.5 - 59° for both compounds), mixed m.p. (58.5 - 59°) and infra-red spectrum. Agerathochromene is therefore 6:7-dimethoxy-2:2-dimethylchromene.



I

After our work was finished, and published as a short communication[17], R. Huls[18] synthesized ageratochromene. He used the following reaction scheme:



I II

He started with 1:2:4-trimethoxy-benzene instead of 3:4-dimethoxy-phenol as in our case. From the work of Oliviero and Lugli, Huls observed that in a Friedel-Crafts reaction between polymethoxybenzene and an acid chloride, the acylation is accompanied by a demethylation of the methoxyl group in the ortho position to the ketonic chain.

The melting points obtained by Huls for 6:7-dimethoxy-2:2-dimethyl-Δ^3-chromene and 6:7-dimethoxy-2:2-dimethyl-chroman were 47.5° and 60° respectively. Exactly the same melting points were obtained in our

work for ageratochromene and its dihydrocompound. Ageratochromene and its dihydrocompound also have their ultra-violet maxima at the same wavelengths as the two substances synthesized by Huls, but our extinction values are higher. Our measurements were made in hexane with a Hilger spectrograph. Huls observed his spectra in a Beckman DU spectrophotometer using methanolic solutions of the compounds.

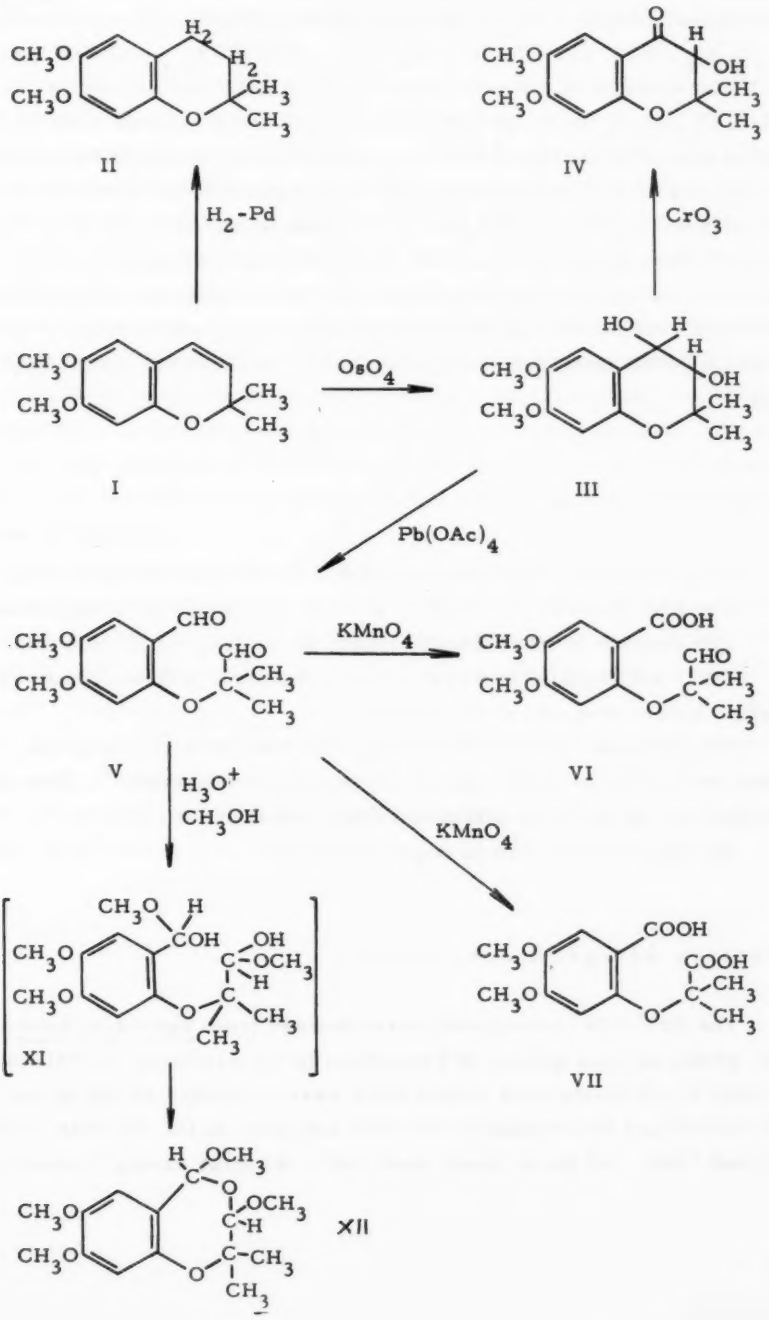
In Table 1 the melting points and ultraviolet maxima are listed for substances which are found both in this work and in that of Huls.

Table 1.

Melting points and ultraviolet maxima for substances synthesized by R. Huls[18] and the same data obtained for a substance isolated from Ageratum houstonianum Mill. and compounds synthesized in this work.

R. Huls	This work	M.p.°	$\lambda_{max.}$ (mμ)
6:7-Dimethoxy-2:2-dimethyl-Δ^3-chromene		47.5	278,322
	Ageratochromene	47.5	280,323
6:7-Dimethoxy-2:2-dimethyl-chroman		60	294
	3:4-Dihydro-ageratochromene	60	293
2-Hydroxy-4:5-dimethoxy-ω-isopropyl-idene-acetophenone		86.5	262,290,361
	2-Hydroxy-4:5-dimethoxy-ω-isopropylidene-acetophenone	79-81	289,358
6:7-Dimethoxy-2:2-dimethyl-chromanone-4		106	238,275,342
	6:7-Dimethoxy-2:2-dimethyl-chromanone-4	103-104	271.5,331

The reactions carried out with the natural substance (I) obtained from Ageratum houstonianum Mill. may be illustrated in the following scheme:



During the recrystallization of (V) an interesting detail was observed. If (V) was treated with methanol containing traces of hydrochloric acid, a crystalline substance (XII) was produced with the elementary composition $C_{15}H_{22}O_6$, m.p. 125-126.5°, and $\lambda_{max.}$ 2820 Å ($\varepsilon_{max.}$ 4000) Figure 4. By X-ray diffraction the molecular weight of (XII) was determined to be 292.7 ($C_{15}H_{22}O_6$ requires 298.3). A Zeisel determination gave the information that (XII) contained four methoxyl groups. Compared with the infrared spectra of ageratochromene and its derivatives, the spectrum of (XII) had only few maxima. (XII) gave no maxima in the carbonyl or hydroxyl region. The ultraviolet spectrum indicated a nonconjugated benzene ring. (XII) could not be oxidized with potassium permanganate. A hemiacetal formation between (V) and methanol probably had occurred, and a subsequent ring closure by dehydration would then have stabilized the product as (XII).

4. EXPERIMENTAL PART

The ultraviolet absorption spectra were measured with a Hilger spectrograph. Hexane was used as solvent unless otherwise specified.

The petroleum ether usually refers to the fraction of b.p. 40 - 70°.

Ether solutions were dried, when necessary, with anhydrous sodium sulphate before removal of the solvent.

The alumina used for chromatography was of technical grade, containing some alkali, which was removed with ethyl acetate[19]. Then the alumina was washed with petroleum ether and dried at 100°.

All temperatures are in degrees Celsius.

4.1. Isolation of ageratochromene.

The first oils investigated were obtained from Ageratum houstonianum Mill. grown on open ground at Trondheim in the summers of 1951 and 1952, but most of the plants used in this work were cultivated by the municipal park authorities of Trondheim and Oslo and given to the Institute in October 1953 and 1954. All these plants were collected after having frozen during

cold nights in the autumns. A small sample of A. houstonianum was kindly given to me by the head gardener of Stadsgartnerens Kontor, Copenhagen, Mr. O. Olsen. These plants were gathered in July 1953 and dried before use.

The plants were distilled with steam. In 1951 and 1952 the plants were divided into two parts, the root and the rest of the plant. Bu: later on, when ageratochromene had been found in both these parts, he whole plant was steam distilled. Large quantities were distilled in our pilot plant distillation apparatus. This procedure gave a much lower yield of oil. When small quantities were distilled the weight of the distillate collected was about three times the weight of the plant material. In the pilot plant apparatus, batches of 30 - 40 kg were distilled and about 40 l distillate was obtained each time, the distillation lasting about 7 hours. The distillates were extracted with petroleum ether, and the combined extracts were dried with anhydrous sodium sulphate overnight. The solvent was then removed by distillation on a water bath in an inert atmosphere. The last traces of petroleum ether were evaporated with a fine stream of nitrogen.

Ageratochromene did not crystallize easily. Oils obtained from the pilot plant distillation, as a rule, had to be purified by high vacuum distillation at 39 - 80°, 10^{-4} mm Hg. The oils were placed in the cold at -10 to -20°, and they very often had to be seeded to induce crystallization.

During chromatography of the oil on alumina the following eluents were used: 1) petroleum ether, 2) 25% and 3) 50% benzene in petroleum ether, 4) benzene and 5) ether. Ageratochromene was found in fractions eluted with 2 and 3.

Table 2.

Time and place of collection of plants, with yields of essential oils and of ageratochromene.

Time of harvesting and distillation	Species	Source of plants	Part of plant	Weight	Ess. oil o/oo	Ageratochromene % of oil
1951	Ageratum houstonianum	Open ground, NTH, Trondheim	Leaves, stems, flowers	610g	1.8[a]	
			Roots	51g	1.6[a]	
Nov. 1952	Ageratum houstonianum	Open ground, NTH, Trondheim	Leaves, stems, flowers	612g	5.0	
			Roots	96g	5.6	
July Aug. 1953	Ageratum houstonianum	Park authorities, Copenhagen	Material dried in air 20-30° Whole plant	550g	6.5[b]	19
Oct. 1953	A. conyzoides	Open ground, NTH, Trondheim	Whole plant	100kg	0.7	
	A. houstonianum					
	A. houstonianum	Park authorities, Trondheim				
Oct. 1954	A. houstonianum	Park authorities, Trondheim and Oslo	Whole plant	226kg		

a. Distillations done by Mr. Magne Nestvold.

b. Yield calculated on dried material.

Owing to the small capacity of the high vacuum still, only small portions could be distilled at a time, and also the crystals came out very slowly. Consequently the yield is given for one experiment only.

The differences in yield of oil obtained in 1951 and 1952 may be due to different growing conditions of the plants. But the oils in 1952 may also have contained traces of petroleum ether. The time of distillation may influence the yield of oil, as, for instance, Lahey[20] found that by prolonged distillation of Evodia littoralis extended over several days, the yield of evodionol, 2:2-dimethyl-5-methoxy-6-acetyl-7-hydroxy-chromene, was increased considerably.

4.2 Ageratochromene.

Ageratochromene (I) formed colourless needles with m.p. 47.5° from petroleum ether. The substance was odourless and had a harsh taste. (I) could be purified by high vacuum sublimation at 60-80°, 10^{-4} mm Hg. Ageratochromene was readily soluble in most organic solvents as petroleum ether, benzene, ether, acetone and ethanol. It was insoluble in cold, but slightly soluble in hot water. Ageratochromene was assumed not to be an acid since it was insoluble in an aqueous solution of sodium carbonate. Neither was it soluble in a cold or a warm aqueous solution of potassium hydroxide and consequently could not be an ester. It contained no phenolic group, because a water solution of ferric chloride gave no colour with an ethanolic solution of ageratochromene. With tetranitromethane in chloroform it gave a brown colour, indicating at least one double bond in the substance. A concentrated ethanolic picric acid solution, when mixed with ageratochromene, turned deep red, but no crystals could be observed.

Ageratochromene was optically inactive, $[\alpha] < \pm 0.5°$. The determination was carried out in chloroform solution in a 1 dm tube at room temperature.

Analysis:

$C_{13}H_{16}O_3$	Calc.	C 70.9	H 7.3
	Found	C 70.8	H 7.35

The substance contained no nitrogen as determined by the micro-Kjeldahl method[21]. The test of Beilstein[22] for halogen was negative. The ultraviolet absorption spectrum of ageratochromene (Figure 1) had:

$\lambda_{max.}$	2800	3230 Å
$\varepsilon_{max.}$	5500	9200

Ageratochromene with m.p. 44.5-45.5° was unaltered by acetylation with acetic anhydride in pyridine at room temperature overnight. The melting point of the recovered material was 42-45°, and the mixed melting point with the starting material was 44-46°.

Hydrolysis of ageratochromene with potassium hydroxide was performed according to Heyes and Robertson[23], but no acetone could be detected. Evodione, 2:2-dimethyl-6-acetyl-5:7:8-trimethoxy-chromene, resisted hydrolysis with either aqueous or alcoholic potassium hydroxide[24].

Potassium permanganate in acetone (E. Merck p.a.) at room temperature did not attack ageratochromene.

4.3. 3:4-Dihydro-ageratochromene.

Catalytic hydrogenation of ageratochromene furnished a dihydrocompound (II). 23.6 mg ageratochromene was hydrogenated with a 2% Pd-on-barium sulphate-catalyst in ethanol. 2.0 ml (20.2°, 763 mm Hg) hydrogen was consumed, the calculated volume being 2.55 ml for $C_{13}H_{16}O_3$ with one double bond.

The dihydrocompound had m.p. 60° and formed glittering, leaf-shaped crystals. Light absorption: maximum at 2930 Å (ε 6400) Figure 2.

The methoxyl content was determined by the micromethod of Pregl and Roth[25].

Calc. for 2 MeO groups in $C_{13}H_{18}O_3$	27.9 % MeO
Found	28.4 % "

4.4. 3:4-Dihydroxy-ageratochromene.

A solution of 870 mg ageratochromene in 3 ml of dry ether was treated with 1 g osmium tetroxide in 5 ml of dry ether[26]. 0.2 ml of dry pyridine was added, and the reaction mixture with its brown precipitate was left overnight. The osmic ester was separated from the solvent by decantation, dissolved in freshly distilled methylene chloride and decomposed with a 1% potassium hydroxide solution (80 ml) containing 10% of mannitol. The major part of the methylene chloride was distilled off, ether was added, and white crystals separated, the yield being 880 mg or 88 %. The glycol (III) had m.p. 129.5°, and an ultraviolet spectrum ($\lambda_{max.}$ 2925 Å, $\varepsilon_{max.}$ 4300) resembling that of 3:4-dihydro-ageratochromene (Figure 2).

A microanalysis was carried out at the Laboratorium voor organische Scheikunde der Universiteit van Amsterdam, Microanalytische Afdeling:

Calc. for $C_{13}H_{18}O_5$	C 61.4	H 7.15
Found	C 61.35	H 7.1

(III) was not attacked by potassium permanganate in acetone (E. Merck p.a.).

Acetylation of 32 mg of the glycol was performed in a mixture of 1 ml pyridine and 1 ml acetic anhydride overnight at room temperature. 10 ml of water, containing one drop of concentrated sulphuric acid, was added to the reaction mixture. The neutral fraction was dissolved in ether, and the ether solution was washed with an aqueous saturated solution of sodium carbonate. After evaporation of the major part of ether, white crystals (14 mg) were obtained. They had m.p. 130° and mixed m.p. with the glycol 110°. In this case it was not possible by elementary analysis to determine whether the substance contained one or two acetyl groups.

Calc. for $C_{13}H_{17}O_5(COCH_3)$	C 60.8	H 6.8
$C_{13}H_{16}O_5(COCH_3)_2$	C 60.35	H 6.55
Found	C 60.55	H 6.65

A methoxyl determination gave the following result:

Calc. for $(CH_3O)_2C_{11}H_{11}O_3(COCH_3)$	20.95 % MeO
$(CH_3O)_2C_{11}H_{10}O_3(COCH_3)_2$	18.35 % MeO
Found	20.05 % MeO

4.5. Oxidation of 3:4-dihydroxy-ageratochromene (III) with sodium dichromate.

146 mg of sodium dichromate in 2 ml of acetic acid was added to

a solution of 374 mg of 3:4-dihydroxy-ageratochromene in 2 ml of acetic acid, the amount of active oxygen corresponded to one gram atom per mol of (III). The solution became deep red. After standing at room temperature (20-25°) overnight the acetic acid was removed by vacuum distillation (10-15 mm Hg), acetone was added, and the chromic salts were filtered off. The acetone was then removed by evaporation in a vacuum, the green oil was dissolved in ether, and from this solvent crystals separated. The yield was 55 mg after purification by high vacuum sublimation at 60-83°, 10^{-4} mm Hg. After recrystallization from ether, the pale yellow crystals had m.p. 118.8-120°, depressed to 99.5-102° on admixture with the glycol (III).

Elementary analysis:

$C_{13}H_{16}O_5$ (IV)	Calc.	C 61.9	H 6.4
	Found	C 61.2	H 6.7

The ultraviolet spectrum had four maxima (Figure 3):

$\lambda_{max.}$	2420,	2745,	3375,	3485 Å
$\varepsilon_{max.}$	55200,	13500,	7600,	6500

An ethanolic solution of the compound (IV) gave no colour with an aqueous solution of ferric chloride.

4.6. Oxidation of 3:4-dihydroxy-ageratochromene (III) with lead tetra-acetate.

Lead tetra-acetate was prepared according to a method given by Fieser[27]. A solution of 3:4-dihydroxy-ageratochromene (III) (830 mg, 3.26 mmol) in acetic acid was treated with lead tetra-acetate (3.3 mmol). After 24 hours at room temperature (20-25°) all the tetra-acetate had reacted, as shown by the failure of the mixture to colour a paper wetted with a potassium iodide-starch solution. The acetic acid was distilled off in a vacuum, water (25 ml) was added, and the solution was extracted three

times with ether. The ethereal solution (about 100 ml) was washed with 10 % aqueous sodium carbonate (5 ml) and aqueous sodium hydrogen carbonate (5 ml). The major part of the ether was distilled off, and white crystals separated in a yield of 520 mg, i.e. 63 %. After recrystallization from ether the substance (V) had m.p. 101.5-102° and was odourless and tasteless. (V) could also be purified by high vacuum sublimation at 80° and 10^{-4} mm Hg. The analysis gave the following results:

$C_{13}H_{16}O_5$	Calc.	C 61.9	H 6.4	MeO 24.6	(2 MeO)
	Found	C 61.5	H 6.5	MeO 25.1	

The ultraviolet absorption spectrum had two maxima (Figure 4):

$\lambda_{max.}$	2730	3160Å
$\varepsilon_{max.}$	15200	7700

(V) formed a 2:4-dinitrophenylhydrazone. It was obtained by dissolving 20.9 mg of (V) in 0.5 ml of methanol (E. Merck p.a.) and adding a solution of 16.5 mg of 2:4-dinitrophenylhydrazine in 2 ml of methanol p.a. acidified with two drops of concentrated hydrochloric acid. Beautiful red crystals separated immediately. They were recrystallized from methanol p.a. and had m.p. 213-216°. The ultraviolet absorption spectrum was determined in chloroform with a Beckman DU spectrophotometer and had a maximum at 3980 Å. An attempt was made to purify the hydrazone by chromatography on alumina, but it could not be eluted with benzene, only with methanol.

When the oxidation of (III) with lead tetra-acetate was first performed, the reaction product was crystallized from methanol, technical grade, and white crystals (XII) separated with m.p. 125-126.5°, depressed to 89-99° on admixture with (V). Further investigations showed that the methanol contained impurities, probably of acidic character. (V) could be recrystallized from pure methanol (E. Merck p.a.) without transformation. When using methanol (E. Merck p.a.) containing traces of hydrochloric acid, white needles separated with m.p. 120.5-123.5°, undepressed on admixture with (XII).

The ultraviolet spectrum of (XII) had a maximum at 2820 Å ($\varepsilon_{max.}$ 4000) Figure 4. Elementary analysis and methoxyl-determination gave these results:

$C_{15}H_{22}O_6$	Calc.	C 60.4	H 7.45	MeO 41.6	(4 MeO)
	Found	C 60.4	H 7.7		
		C 61.0	H 7.6	MeO 39.6	

Prior to the elementary analysis the substance used in the first determination was sublimed at approximately 90° and 0.1 mm Hg.

(XII) was soluble in ether, slightly soluble in methanol and in ethanol, but insoluble in cold and hot water. It gave no colour reaction with ferric chloride. The acetal test[28] was negative. (XII) could not be oxidized by potassium permanganate, neither when dissolved in acetone nor suspended in water.

The molecular weight (M) of (XII) was determined by X-ray diffraction, using the formula:

$$M = \frac{V\,d\,N}{n}$$

V: volume of the elementary cell, [x]
d: specific gravity,
N: Avogadro's number,
n: number of molecules in the elementary cell.

The density of (XII) was found by suspending its crystals in solutions of varying specific gravity. The crystals remained suspended in a solution of potassium iodide and sodium thiosulphate of density 1.276 g/cm^3 even after centrifugation.

---

[x] The determination of the volume V of the elementary cell was made by Cand. real. Paul Øyum, at that time at Institutt for teoretisk kjemi, NTH.

(XII) formed needle-like crystals, and the elementary unit cell was found to be monoclinic with the c-axis parallel with the axis of the needle. Oscillation- and Weissenberg-diagrams about the b- and c-axis gave the dimensions:

$a = 7.24$ Å
$b = 20.36$ Å
$c = 10.36$ Å
$\beta = 94^{\circ}$
$V = 1523.46$ Å^3
$n = 4$

The molecular weight

$$M = \frac{V\,d\,N}{n} = \frac{1523.46 \times 1.276 \times 6.023.10^{23}}{4 \times 10^{24}} = \underline{292.7}$$

Calc. for $C_{15}H_{22}O_6$ $\underline{298.3}$

4.7. Oxidation of (V) with potassium permanganate. The monocarboxylic acid.

The carbonylic compound (V), obtained from the glycol by oxidation with lead tetra-acetate, could be oxidized further with potassium permanganate to a monocarboxylic acid (VI).

A solution of 420 mg of (V) in 10 ml of acetone was treated with an acetone solution of 176 mg of $KMnO_4$, corresponding to one gram atom of oxygen per mole of (V). To keep the solution from being too alkaline, solid magnesium sulphate was added[29]. After 24 hours at room temperature (20-25°) the major part of the acetone was distilled off, and water and 5 ml of an aqueous solution of sulphur dioxide were added. The organic material was extracted with ether (250 ml), and the ethereal solution was shaken with aqueous sodium carbonate (2x10 ml). Only traces of organic material remained in the ethereal solution. After acidification of the aqueous solution with dilute sulphuric acid (2 ml of 50 % H_2SO_4), the organic acid was extracted with ether (total volume 280 ml). The main part of the ether was distilled off, and crystals separated. After recrystallization from anhydrous ether the faintly yellow needles (VI) had m.p.

118-119°. Yield of (VI): 108 mg, 24 %.

$C_{13}H_{16}O_6$ Calc. C 58.2 H 6.0

Found C 57.95 H 6.0

Before analysis the substance was dried over P_2O_5 at 75° in a vacuum for 48 hours.

Light absorption in ethanol (Fig. 5):

$\lambda_{max.}$ 2745 3320

$\varepsilon_{max.}$ 8500 5400

The acid was soluble in ether, chloroform and ethanol, but insoluble or only slightly soluble in petroleum ether. It dissolved readily in aqueous sodium carbonate and sodium hydrogen carbonate and was slightly soluble in water. It gave no colour reaction with ferric chloride.

11 mg of the monocarboxylic acid (VI) was dissolved in 0.5 ml of methanol (E. Merck p.a.). To this solution was added 10 mg of 2:4-dinitrophenylhydrazine in 2 ml of methanol p.a., acidified with two drops of concentrated hydrochloric acid. Deep red crystals separated. After recrystallization from methanol p.a. the 2:4-dinitrophenylhydrazone had m. p. 210-212°, depressed to 172-182° on admixture with 2:4-dinitrophenylhydrazine. An attempt was made to purify the hydrazone by chromatography on alumina, but it could not be eluted with benzene. The ultraviolet absorption spectrum of the 2:4-dinitrophenylhydrazone was measured in chloroform with a Beckman DU spectrophotometer:

$\lambda_{max.}$ 4020 Å, $\varepsilon_{max.}$ 28350.

4.8. The dicarboxylic acid.

145 mg of (V) in 2 ml of acetone was added to a solution of 174 mg of potassium permanganate in 20 ml of acetone. The amount of $KMnO_4$ corresponded to 3 gram atoms of oxygen per mole of (V). The acetone used had been purified by distillation over potassium permanganate.

After 24 hours at room temperature (20-25°) the acetone was evaporated, and the manganese dioxide was dissolved in 15 ml of an aqueous solution of sulphur dioxide. The acid was then extracted with 120 ml of chloroform. The chloroform was distilled off, giving white crystals in a deep-green liquid. After recrystallization from chloroform-ether the substance (VII), 58 mg, 35 %, had m.p. 157-159.5°. Earlier experiments had shown that only traces of neutral material could be found in the reaction mixture. The reaction could also be carried out in an aqueous solution to give the same dicarboxylic acid.

(VII) dissolved readily in chloroform, but was only slightly soluble in ether, petroleum ether and cold water. It was soluble in hot water. The substance had a slightly acid taste.

$C_{13}H_{16}O_7$	Calc.	C 54.9	H 5.65	MeO 22.0	(2 MeO)
	Found	C 54.6	H 5.45	MeO 22.5	

For elementary analysis the substance was dried over P_2O_5 at 75° in a vacuum for 24 hours.

The ultraviolet absorption spectrum was measured in ethanol (Fig. 5):

$\lambda_{max.}$	2570	2990 Å
$\varepsilon_{max.}$	13000	7100

(VII) was found to be unchanged on boiling on a water-bath for one hour with a 6 % alcoholic potassium hydroxide solution. It did not react with 2:4-dinitrophenylhydrazine, but the dicarboxylic acid gave a reddish brown colour with ferric chloride. (VII) could be purified by high vacuum sublimation at 135-140°, 10^{-4} mm Hg. The melting point of the sublimate was 159-163°. If the melt was allowed to cool, it crystallized, and on heating again a new m.p. was observed at 172-174°.

A destructive distillation of the dicarboxylic acid (27 mg) was tried at 10 mm Hg and a temperature below 218°. At 178° white crystals sublimed. They had m.p. 190-195° and light absorption $\lambda_{max.}$ 3220 Å, log $E^{1\%}_{1cm}$ 2.55. The gases evolved were absorbed in Ascarite, weight increase 10.5 mg, and Dehydrite, weight increase 1.4 mg. If two carbon dioxide groups were given off from the dicarboxylic acid, the increase in weight of the Ascarite absorbent had been 8.4 mg.

The dicarboxylic acid as obtained from (V) by oxidation with $KMnO_4$ [3 0] dissolved readily in chloroform. However, when the oxidation residue was extracted once more with chloroform and this extract evaporated separately, a few milligrams of white crystals were left. They were only slightly soluble in chloroform, but readily dissolved in ether. The substance gave a reddish-brown colour with ferric chloride. After recrystallization from ether-chloroform the crystals had m.p. 175-176.3°, depressed to 160-164° on admixture with hemipinic acid, m.p. 169-171°. The melting points were all taken at the same time. The m.p. was also depressed (to 163-168°) on admixture with m-hemipinic acid, 4:5-dimethoxy-phthalic acid, (m.p. 175-177°), but unfortunately the last determinations were carried out separately. Owing to lack of material this byproduct could not be investigated further.

5. SYNTHETIC SUBSTANCES

5.1. Phenoxyacetone.

Phenoxyacetone was prepared by the Williamson synthesis which involved the interaction of bromoacetone and sodium phenoxide[30]. The bromoacetone used had b.p. 38-51° (16-17 mm Hg) and was obtained by a direct bromination of acetone[31]. Before any determination of physical properties were made, the phenoxyacetone was shaken with an aqueous solution of potassium hydroxide (2 N) in order to remove phenolic impurities. The reaction product had b.p. 102-104° (9-10 mm Hg) and $n_D^{21.5}$ 1.5188. The data for phenoxyacetone given in the literature[32] were 110-112° (12 mm Hg) and n_D^{20} 1.5228, respectively. The infra-red spectrum was measured (Figure 16).

$C_6H_5OCH_2COCH_3$ Calc. C 72.0 H 6.7

Found C 71.7 H 6.55

After standing for a long time at -20°, phenoxyacetone crystallized.

5.2. Phenoxyglycerol.

A procedure given in Organic Syntheses[33] was followed. Sodium phenoxide reacted with glycerol α-chlorohydrin giving a compound with b.p. 120-132° (2.5 mm Hg) and 126-130° (2 mm Hg). Organic Syntheses gives b.p. 175-190° (15 mm Hg).

After recrystallization from chloroform-dry ether the white crystals had m.p. 56-58°. An alcoholic solution of the substance gave no colour with an aqueous solution of ferric chloride. Lange's Handbook[34] gives the m.p. 69-70°, or 53-54° when the substance contains traces of impurities.

5.3. Phenoxyacetaldehyde.

Phenoxyglycerol (0.075 moles) was oxidized with lead tetra-acetate in benzene according to a procedure given by Speer and Mahler[35]. They fractionated their product through a 24-inch Widmer column and obtained the b.p. 82-83° (4-5 mm Hg). Using a Claisen flask phenoxyacetaldehyde distilled at 64° (4 mm Hg). The refractive index was n_D^{20} 1.5318, literature n_D^{20} 1.5360. The infra-red spectrum was recorded (Figure 17).

Phenoxyacetaldehyde 2:4-dinitrophenylhydrazone was purified by chromatography on alumina. After recrystallization from chloroform-methanol the cube-shaped crystals had m.p. 136-138°, literature 138° [36]. The ultraviolet spectrum was measured in a Beckman DU spectrophotometer in chloroform solution, $\lambda_{max.}$ 3480 Å, $\varepsilon_{max.}$ 28200.

$C_6H_5OCH_2CH = N . NH . C_6H_3(NO_2)_2$

Calc.	C 53.15	H 3.8
Found	C 53.05	H 3.9

5.4. Hemipinic acid; 3:4-dimethoxy-phthalic acid.

On oxidative hydrolysis narcotine, $C_{22}H_{23}O_7N.HCl.H_2O$ (20 g), was broken down to cotarnine and opianic acid[37]. The yield of opianic acid, 5:6-dimethoxy-phthalaldehydic acid, was 4.4 g (49 %), m.p.

144-146°, Wegscheider and Späth[38] give 147-148°. They found that the melting point 150° published earlier by one of them[37] probably was too high. Opianic acid (4.4 g) was heated on a steam bath with an approximately 30 per cent solution of potassium hydroxide in water[39]. The yield of meconin, 5:6-dimethoxy-phthalide, was 0.8 g (39 %), m.p. 98-99°, literature[39] 102-103°. Yield of hemipinic acid 0.32 g, 14 %; Rodionow et al.[39] obtained a yield of 77 %, based on the opianic acid. After recrystallization from water, the white prisms had m.p. 160-161°, not depressed on admixture with the dicarboxylic acid (VII), m.p. 162-163°; all three samples were measured at the same time.

Hemipinic acid could not be dissolved in chloroform or carbon disulphide, even if the water of crystallization had been removed by sublimation in a high vacuum at 110-120°, 10^{-4} mm Hg. The infra-red spectra of meconin and hemipinic acid were measured (Figures 18 and 19).

5.5. m-Hemipinic acid; 4:5-dimethoxy-phthalic acid.

5 g of emetine hydrochloride ($C_{29}H_{40}O_4N_2.2HCl.7H_2O$) was oxidized with potassium permanganate. When the instructions given by Windaus and Hermanns[40] were followed, faint yellow crystals separated, m.p. 317.5-320°. m-Hemipinic imide has m.p. 318-320° [40]. The product was saponified with 20 ml of alcoholic potassium hydroxide (6 g KOH-100 ml ethanol) with heating on a steam bath for one hour. The ethanol was evaporated, water was added, and the solution was acidified with concentrated hydrochloric acid and extracted with ether. Faintly yellow crystals with m.p. 180-183° separated after evaporation of some of the ether. On moderate heating m-hemipinic acid melts at 179-182° [41]. The yield of acid was 330 mg, 10 %; Windaus and Hermanns obtained 35 % based on emetine hydrochloride.

m-Hemipinic acid was sublimed in a high vacuum at 120-140°, 4.10^{-4} mm Hg. The white crystals had m.p. 175-177°, depressed to 163-168° on admixture with the substance of m.p. 175-176.3° and slightly soluble in chloroform, obtained by oxidation of (V) with potassium permanganate [30]. The melting points were taken separately.

The infra-red spectrum was recorded (Figure 20).

5.6. α-Bromoisovaleric acid.

Isopropylmalonic ester was prepared by the method used for n-butylmalonic acid[42]. The yield of product boiling at 96-100° at 12.5-13 mm Hg was 71 per cent of the theoretical amount. n_D^{20} 1.4165, literature n_D 1.418[43]. α-Bromoisovaleric acid was synthesized by saponification, bromination and decarboxylation of the ester[44]. The yield of acid boiling at 120-125° at 13-15 mm Hg was 54 per cent based on the isopropylmalonic ester.

5.7. ββ-Dimethylacrylic acid.

A mixture of 40 g of α-bromoisovaleric acid and 80 g of quinoline was heated and, when the vigorous reaction had ceased, maintained at 165-170° for 20 minutes[45]. After the addition of excess of dilute hydrochloric acid to the cooled reaction mixture ββ-dimethylacrylic acid was extracted with ether and purified by distillation in a vacuum at 86-94° and 13 mm Hg. Yield 7 g, 32 %, given value 11.5 g, 52 %. Recrystallization from petroleum ether gave a product melting at 63-66°, Bridge et al.[45] give 67-68°.

5.8. ββ-Dimethylacryl chloride.

6 g of ββ-dimethylacrylic acid was gently heated with 6.5 ml of thionyl chloride (purified according to Fieser[46]). By distillation at 47-50° (14 mm Hg) ββ-dimethylacryl chloride was obtained, the yield was 4.7 g (66 %). Bridge et al.[45] reported a 77 % yield of material, distilling at 45-48° (12 mm Hg).

5.9. 5:7-Dihydroxy-2:2-dimethylchromanone.

A mixture of 82 ml of nitrobenzene and 6.7 g of phloroglucinol was agitated and 6.2 g of aluminium chloride was dissolved in it[45]. 4.7 g of

ββ-dimethylacryl chloride was then introduced gradually, and the reaction mixture was kept at room temperature (20-25°) for 4 days. After the addition of 100 g of ice and 50 ml of hydrochloric acid (20 ml of concentrated HCl diluted with water to 80 ml), the product was extracted with ether, the ether was evaporated, and the nitrobenzene was removed by means of steam. The cooled aqueous solution slowly deposited the chromanone as needle-shaped crystals, yield 1.75 g, 21 %; Bridge et al.[45] obtained 71 per cent of the theoretical amount. The substance could be purified by high vacuum sublimation at 90-100° and 5.10^{-5} mm Hg. The product obtained melted at 193-195° (literature 198°). The compound in ethanol gave a reddish violet colour with aqueous ferric chloride. The infra-red spectrum is given in Figure 21.

5.10. 5:7-Dihydroxy-2:2-dimethylchroman.

Amalgamated zinc was prepared according to Barton et al.[47]. 40 g of mercuric chloride was dissolved in 150 ml of water by heating. 150 ml of abs. ethanol was added, and 40 g of zinc wool was soaked in the solution which was agitated for a few minutes. The ethanolic solution then was decanted.

The reduction[45] of 1 g of 5:7-dihydroxy-2:2-dimethylchromanone gave 300 mg (32 %) of the corresponding chroman which crystallized from benzene with m.p. 149-150°. The melting point was unchanged after sublimation at 90-100°, 5.10^{-5} mm Hg. In the literature the yield is given as 64 % with m.p. 162-163° after crystallization from benzene and then from water. An alcoholic solution of ferric chloride gave a faint blue colour with the 5:7-dihydroxy-2:2-dimethylchroman, but with aqueous ferric chloride the reaction was negative. The infra-red spectrum is given in Figure 22.

5.11. 5:7-Dimethoxy-2:2-dimethylchroman.

Methylation of 5:7-dihydroxy-2:2-dimethylchroman (300 mg) was effected with methyl iodide and potassium carbonate in boiling acetone[16].

Distillation of the residual oil in a high vacuum at 10^{-5} mm Hg gave the 5:7-dimethoxy-2:2-dimethylchroman as an almost colourless oil with b.p. 60-70°. When chromatographed on alumina the substance was eluted with 10 per cent benzene in petroleum ether.

The infra-red spectrum had no maximum in the carbonyl region (Figure 23). Robertson and Subramaniam[16] obtained 5:7-dimethoxy-2:2-dimethylchroman as an oil with b.p. 105-106° at 0.05 mm Hg.

5.12. Veratronitrile.

Veratraldehyde was treated with hydroxylamine hydrochloride, giving veratraldoxime, which was heated with acetic anhydride, forming veratronitrile in 58 % yield[48]. The veratronitrile melted at 63-65°, literature 66-67°.

5.13. 4-Aminoveratrole; 3:4-dimethoxy-aniline.

A method given in Organic Syntheses was followed[49]. 47 g of veratronitrile was used as starting material, giving 4-aminoveratrole, b.p. 168-172° at 18 mm Hg, in 61 % yield.

5.14. 3:4-Dimethoxy-phenol.

For the synthesis of 3:4-dimethoxy-phenol a procedure reported by Alexander Robertson and collaborators[50] was used with modifications. 17.5 g of 4-aminoveratrole dissolved in 275 ml of water and 30 ml of concentrated sulphuric acid was diazotized at -10° with 16 % aqueous sodium nitrite (50 ml). The filtered liquid was gradually added to 2 litres of boiling water. The solution was boiled for 5 minutes with vigorous mechanical stirring and nitrogen bubbling through the liquid. After cooling, the solution was extracted several times with ether. The product left on evaporation of the combined ether extracts was purified by distillation in a high vacuum, the distillate was crystallized from carbon

tetrachloride, and the crystals were sublimed in a high vacuum at 60-70° and 2-3.10^{-4} mm Hg. The 3:4-dimethoxyphenol melted at 77-80°. The ferric chloride reaction in water was bluish-green, instantly changing to reddish-brown. The yield of 3:4-dimethoxy-phenol, not completely purified, was 7.3 g, 42 %. The infra-red spectrum of the pure material was measured (Figure 24).

5.15. 6:7-Dimethoxy-2:2-dimethylchromanone.

8.5 g of 3:4-dimethoxy-phenol in 100 ml of nitrobenzene was stirred, and 7.5 g of aluminium chloride was added. To this solution 5.3 g of $\beta\beta$-dimethylacryl chloride was gradually introduced, and the reaction mixture was kept at room temperature for 4 days. Then 75 g of ice and 50 ml of hydrochloric acid (20 ml of concentrated acid diluted with water to 80 ml) was added, and the product was isolated with ether. After evaporation of the ether, the nitrobenzene was removed by means of steam. The aqueous solution was extracted with ether, the ether was distilled off, and the product was further purified by high vacuum sublimation at 90-110° and 10^{-4} mm Hg. A mass of yellow crystals sublimed into the cooler part of the sublimation apparatus. Above 100° colourless crystals (150 mg) were formed on the upper part of the sublimation bulb which was heated in an air bath. They had m.p. 156-157.5°. The infra-red spectrum was measured (Figure 25). The intensity of the carbonyl absorption at 1645 cm^{-1} was weak compared with the other maxima. The substance was not investigated further.

By chromatography on Floridin XXX the yellow crystalline mass was separated into two substances. Yellow crystals were eluted with petroleum ether, and white crystals with ether.

The white crystals had m.p. 103-104° and gave no colour reaction with ferric chloride. The substance could be dissolved in 10 per cent aqueous sodium hydroxide. The ultraviolet absorption spectrum had two maxima (Figure 6):

$\lambda_{max.}$	2715	3310 Å
$\varepsilon_{max.}$	16300	7600

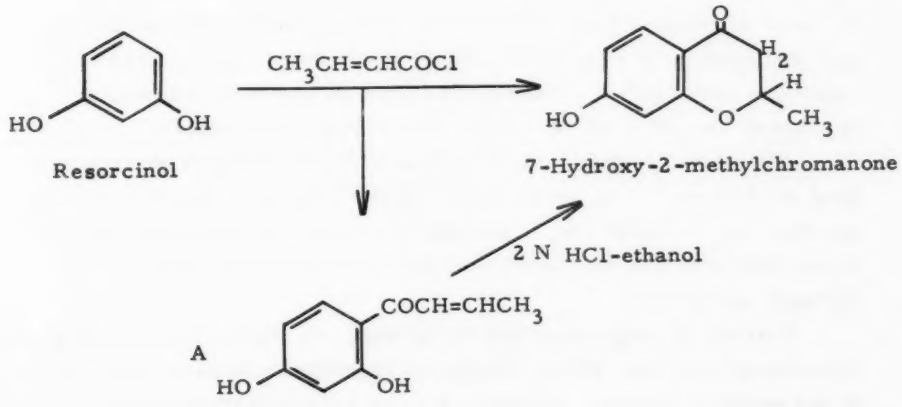
The infra-red spectrum was recorded (Figure 27).

The yellow substance was sublimed in a high vacuum at 50-60°, 10^{-4} mm Hg, forming needles on the glass wall of the bulb in the air-bath. The yellow needles melted at 79-81° and gave a green colour with ferric chloride. (Figure 6):

$\lambda_{max.}$ 2890 3580 Å

$\varepsilon_{max.}$ 16800 10900

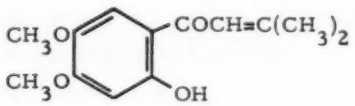
The yellow substance could also be dissolved in 10 % aqueous sodium hydroxide, but after a minute, white crystals separated, which had m.p. 102-103°. This suggested a conversion similar to the one observed by Alexander Robertson and collaborators[51]. They attempted to synthesize 7-hydroxy-2-methylchromanone by a Friedel-Crafts reaction using resorcinol and crotonyl chloride and obtained a mixture of two substances. The chromanone formed white crystals. They also isolated a yellow ketone which in all probability had formula A since on cyclization it was quantitatively converted into the isomeric chroman-4-one.



Consequently the same conversion was now tried with our yellow substance. It was boiled for two hours with a mixture of 50 ml of hydrochloric acid (2N) and 10 ml of ethanol (96 per cent). On standing overnight at room temperature white crystals separated. They melted at

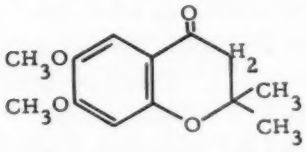
102-103°, and the melting point was not depressed on admixture with the white crystals obtained by the Friedel-Crafts reaction directly.

The yellow crystals with m.p. 79-81° was analysed:



Calc. C 66.1 H 6.85
Found C 66.5 H 6.8

Before elementary analysis was carried out, the white crystals were dried over phosphorous pentoxide at 60° in a vacuum.



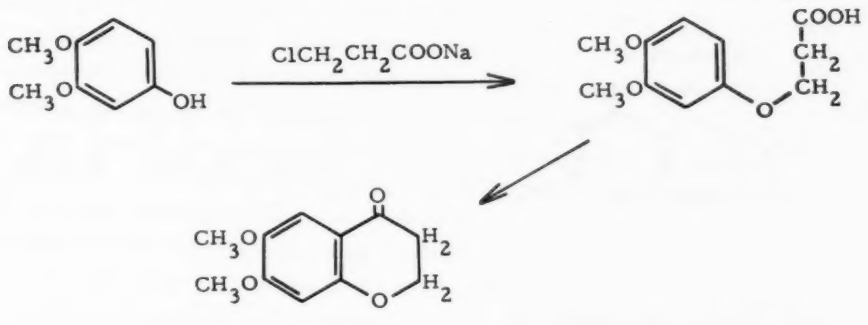
Calc. C 66.1 H 6.85
Found C 66.5 H 6.8

The assumption that the yellow substance had the formula written above was confirmed by the infra-red spectrum (Figure 26). It showed a strong absorption band at 1640 cm^{-1}. Benzal acetophenone absorbs at 1667 cm^{-1} owing to the conjugation of the CO group with an aliphatic double bond and an aryl ring[52]. The 2-hydroxy-aryl ketone has an infrared absorption band at 1655-1635 cm^{-1}, modified also by the nature and position of ring substituents. It is possible that the 1640 cm^{-1} maximum of the yellow substance has been shifted from the normal position by the influence of both the above mentioned features.

The white crystals, the chromanone, had a carbonyl absorption band at 1675 cm^{-1}. An aryl ketone, Ph-CO-, has an infra-red absorption band at 1700-1680 cm^{-1}, and the frequencies of a carbonyl group in an unstrained six-membered ring are the same as for open chain carbonyl compounds.

Both of the ortho-positions being free, the reaction between 3:4-dimethoxyphenol and ββ-dimethylacryl chloride could have taken either of two possible courses, forming a 6:7- or a 5:6-dimethoxy-2:2-dimethylchromanone. The former was the more probable since here there was no steric hindrance (compare the synthesis of 7-hydroxy-2-methylchromanone[51]). By the condensation of 3:4-dimethoxyphenol with β-chloropropionic acid, the only substance, in addition to 6:7-

dimethoxy-chroman-4-one, which Alexander Robertson and collaborators[50] isolated, was unchanged acid.



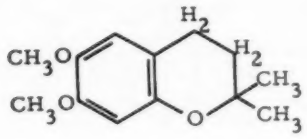
5.16. 6:7-Dimethoxy-2:2-dimethylchroman.

A solution of 6:7-dimethoxy-2:2-dimethylchromanone (250 mg) in a mixture of ethanol (2.5 ml), acetic acid (1.25 ml), water (5 ml) and concentrated hydrochloric acid (4 ml) was kept at room temperature for 2 days in contact with 10 g of amalgamated zinc wool (prepared according to Barton et al.[47]). The reduction of the carbonyl function was made as in the synthesis of 5:7-dimethoxy-2:2-dimethylchroman[45]. The mixture was treated with 12 % hydrochloric acid (4 ml) and heated on the steam-bath for one hour. More acid (4 ml) was then added, and the mixture was refluxed for $7\frac{1}{2}$ hours. The cooled solution was decanted and extracted several times with ether. The combined extracts were washed well with aqueous sodium bicarbonate and dried, and the ether was evaporated. The residue was dissolved in ether-petroleum ether, and on cooling the 6:7-dimethoxy-2:2-dimethylchroman separated as white needles. After recrystallization the chroman had m.p. 58.5-59°, undepressed on admixture with 3:4-dihydro-ageratochromene (m.p. 58.5-59°). The melting points of the two compared substances and their admixture were taken all at the same time.

The infra-red spectrum of the 6:7-dimethoxy-2:2-dimethylchroman was identical with that of the 3:4-dihydro-ageratochromene (Figure 8).

The 6:7-dimethoxy-2:2-dimethylchroman was sublimed in a high

vacuum at 45-55°, 5.10^{-4} - 5.10^{-5} mm Hg.



Calc.	C 70.25	H 8.15
Found	C 69.8	H 7.85

6. THE INFRA-RED SPECTRA

A Perkin-Elmer Model 21 double beam spectrophotometer equipped with NaCl optics was used for the infra-red determinations. Immediately after each run the wave-length scale was checked with the 1495 cm^{-1} band of a thin film of polystyrene. The spectra of about 20 substances including 9 substituted benzopyrans were obtained. In the present investigation an attempt has been made to relate the infra-red absorption bands with structural units of substituted chromans and benzene derivatives. A critical review of the data on which infra-red spectral correlations are based, has been made by Bellamy[52], and his book has been consulted.

Most of the spectra in this work were obtained with substances dissolved in chloroform. Some compounds were studied as liquids and a few as solids in a potassium bromide disc. The changes of state and solvents may result in frequency shifts of the absorption maxima. The shifts, due to different solvents, have been related to some specific property of the liquids such as their dielectric constants. Bellamy, Hallam and Williams[53,54] have studied the X-H stretching frequencies and the carbonyl absorptions, and they postulate that the frequency shifts are produced mainly by local association effects; the dielectric constant of the solvents is much less important than has been previously supposed.

When the absorption maxima of the substances measured in this work are described as strong or weak, it only refers to whether the transmission is lower than 20 or higher than 70 %, respectively.

As early as 1905 it was recognized that infra-red absorption bands in the region of 3000 cm^{-1} arise from the C-H stretching modes[55]. The exact positions of the maxima are dependent on the nature of the linkages

involved. But in the region near 3000 cm^{-1} the dispersion of the sodium chloride prism, which has been used in this work, is low. It is therefore not possible to recognize all the various types of the C-H stretching frequencies which arise from the benzopyrans and 1:2:4:5-substituted benzenes. When no more than one maximum near 3000 cm^{-1} is found, it is only possible to observe whether or not the band is symmetrical. Particularly when additional hydroxyl or carboxyl groups are present and hydrogen bonding occurs, the maximum is very broad, owing to overlapping with the OH stretching frequency (Table 3 and 4).

For the last fifteen years it has been known that, owing to hydrogen bending vibrations, a CH_3-group gives rise to two maxima, one in the region near 1460 cm^{-1} and the other near 1375 cm^{-1}. As first noted by Thompson and Torkington[56], a splitting of the symmetrical CH_3 absorption band occurs if two methyl groups are attached to the same carbon atom. With the isopropyl grouping $(CH_3)_2CH$- or $(CH_3)_2CR$- the bands appear at about an equal distance on each side of the mean value at 1385-1350 cm^{-1} and with approximately equal intensities. Bellamy[57] has given two examples of the position of the CH_3 symmetrical deformation frequency when the methyl group is attached to oxygen. Methanol has a maximum at 1456 cm^{-1} and dimethyl ether one at 1466 cm^{-1} which have been correlated with the methyl group. In most cases the absorption frequency of the X-CH_3 group remains relatively constant for any single element X.

The absorption maxima of the substituted benzopyrans are listed in Table 3. Most of the compounds have two maxima in the region 1386-1362 cm^{-1} and coinciding with the given value for the isopropyl grouping. 6:7-Dimethoxy-2:2-dimethyl-chromanone, 5:7-dihydroxy-2:2-dimethyl-chromanone and 6:7-dimethoxy-2:2-dimethyl-3-hydroxy-4-acetoxychroman have only one band. It is not symmetrical but has a distinct shoulder at 1385-1380 cm^{-1}. The intensity of the maximum at 1375 - 1362 cm^{-1} is higher than that of the maximum at 1385 cm^{-1}. The only exceptions are the glycol (III) and its oxidation product, the 6:7-dimethoxy-2:2-dimethyl-3-hydroxy-chromanone (IV). Bellamy gives examples, showing that the two maxima of the isopropyl group have approximately equal intensities.

The absorption at 1465-1455 cm^{-1} is common to all the substituted 2:2-dimethyl-benzopyrans and probably should be associated with

Table 3. Infra-red maxima of substituted benzopyrans.

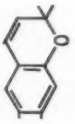
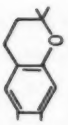
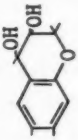
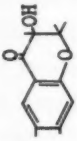
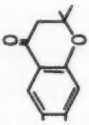
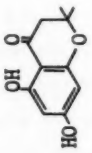
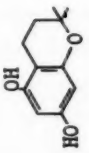
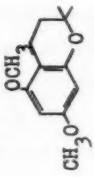
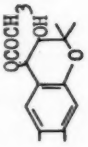
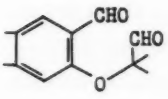
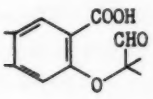
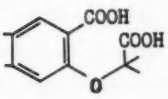
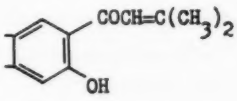
Fig. 7	Fig. 8	Fig. 9	Fig. 11	Fig. 27	Fig. 21	Fig. 22	Fig. 23	Fig. 10
								
I	II	III	IV					VIII
CCl_4	$CHCl_3$	$CHCl_3$	$CHCl_3$	$CHCl_3$	KBr	KBr	Liquid	$CHCl_3$
		3590	3530			3380		3550
		3480				3290		
2980	2950	3040	3050	3020	3150	2950	2970	3020
2950		2975	3020			2900sh		2960sh
			2975					
2840	2855	2855	2860	2870			2875	2850
1640sh*			1682	1675	1643			1745
1620	1626	1628	1622	1620	1600sh	1635	1625	1626
1582	1605	1606	1593	1595	1582	1615	1598	1610
1503	1518	1513	1504	1505	1500	1520	1498	1512
	1470	1470	1472	1472			1468	1470
1465	1455	1458	1462	1460	1462	1462	1458	1456
1444	1448	1448	1445	1442			1445	1445
1422	1415	1415	1430	1428			1425	1418
				1410				
1383	1386	1385	1386	1385sh	1380sh	1385	1385	1385sh
1362	1372	1372	1370	1375	1370	1372	1370	1372
1342	1346					1343	1348	
1318	1325	1328	1328	1320	1330		1325	1312sh
1278	1272	1295	1268	1275	1295	1285	1295	1298
1260	1260	1262			1252	1255	1260	
1243	1240	1240	1240	1240			1236	1240
1213		1225	Plateau	1212		1226	1215	
1195	1195	1195		1196	1192		1202	1195
							1183	1180
1162	1178	1176	1160	1158	1162	1143	1158	1153
	1155	1145					1144	
1135	1122	1125	1136	1106	1120sh	1115	1122	1135
1108		1095	1106		1082		1108	1085
1030	1020	1038	1026	1050		1043	1052	1032
				1033				
1013	1000	1010	996	995	1010	1009	1008	1012
952		970	976	963	958			982
								959
943	938	938					942	942
924	922							928
904	900			912	908		915	912
882	890	887	892	887				892
853	854	856	863	868	872	868	875	853
835		834	838		825			832
	818	818	812		806	814	810	810
					744	747	756	
					730			
709								
678	662	660	660					690
								660

Table 4. Infra-red maxima of 1:2:4:5-substituted benzenes.

Fig. 12	Fig. 14	Fig. 15	Fig. 26
			
V	VI	VII	
$CHCl_3$	KBR	$CHCl_3$	$CHCl_3$
3030	2970	3040	2980
2950			2880
2870			
2720	2630	2650	
2630	2530		
1742	1740	1735	
1676	1675	1688	
	1640		1640
1610	1610	1615	
		1590	1593
1512	1512	1515	1515
1470	1465	1465	1469
1452	1455sh	1450	
1443	1436		1446
1410	1415	1413	
1388	1388sh	1390	1394
1367	1363	1362	1362
1353	1356		
			1313
1272	1275		1278
	1248	1255	1251
1223	1219		1230
1196	1198	1190sh	1202
	1175	1166	1178
1140	1140	1146	1153
1120	1130		
		1077	1077
1032	1033	1032	1032sh
1005	1005	996	1013
			986
	954	950	
918	908		
876	868	878	875
825	822	830	843
	783		
	747		
	718		
662	672	660	

the CH_2 and the CH_3 groups. The dimethoxy compounds except ageratochromene itself, have a second maximum at 1472-1468 cm^{-1}. This maximum may be correlated with the CH_3O group. Two additional bands at 1448-1442 cm^{-1} and 1430-1415 cm^{-1} occur in all the dimethoxy benzopyrans in Table 3, but not in the corresponding dihydroxy compounds.

The absorptions of the substituted benzopyrans follow the correlations for aromatic compounds discussed by Bellamy[58]. The substances listed in Table 3 have two strong absorption maxima in the regions 1520-1498 cm^{-1} and 1635-1620 cm^{-1}. They also have a maximum at 1615-1582 cm^{-1}. When the substances are measured in solution the intensity of the last bond is weak unless the aromatic ring is conjugated with a double bond or a carbonyl group as in ageratochromene or in 6:7-dimethoxy-2:2-dimethyl-chromanone. The stretching vibration of the C=C bond conjugated with the aromatic ring in ageratochromene appears as a shoulder on the high frequency side of the 1620 cm^{-1} band.

The absorption patterns indicated above are followed to a great extent by the 1:2:4:5-substituted benzenes listed in Table 4. The shifts produced by changes of state are very small in these regions.

The out-of-plane deformation vibrations of the hydrogen atoms remaining on the aromatic ring, give rise to absorption in the region 1000-650 cm^{-1}. The work of Dannenberg et al.[59] was consulted when it was attempted to decide in what order the substituents of ageratochromene were arranged. Dannenberg et al. found that 1:2:3:4-substituted aromatic rings have one maximum in the region 820-800 cm^{-1}. From the literature they collected the data that 1:2:3:5- and 1:2:4:5-substituted aromatic rings absorb at higher frequencies, at 885-868 cm^{-1} and 890-853 cm^{-1}, respectively. All the substances listed in Tables 3 and 4 have several maxima between 800 and 900 cm^{-1}, but they all have one maximum in the region 878-853 cm^{-1}. The monocarboxylic acid (VI) (Figure 14, KBr disc) has a maximum at 868 cm^{-1}, but the band at 822 cm^{-1} can hardly be seen. Therefore the 1:2:3:4-arrangement was ruled out, and ageratochromene was proposed to have the two methoxy groups in the 5:7- or 6:7-positions.

The absorption range for the stretching vibration of the free hydroxyl group is quoted as being 3650-3590 cm^{-1}. When inter- or intramolecular hydrogen bonds are formed, the maxima are shifted to higher wavelengths. 5:7-Dihydroxy-2:2-dimethyl-chroman have two strong maxima at 3380 and 3290 cm^{-1}. In the present case the substance has been examined in the

solid state, and in crystals the molecules have orientated themselves in such a way as to give the maximum strength of hydrogen bonds. 6:7-Dimethoxy-3:4-dihydroxy-2:2-dimethyl-chroman (III), its monoacetate (VIII) and the oxidation product, 6:7-dimethoxy-3-hydroxy-2:2-dimethyl-chromanone (IV), absorb in the region 3550-3480 cm^{-1}. The shifts from the normal position at 3650-3590 cm^{-1} makes it possible that the compounds have intramolecular hydrogen bonds. With the yellow substance, 2-hydroxy-4:5-dimethoxy-ω-isopropylidene-acetophenone, it is not easy to recognize the exact position of the hydroxyl maxima. The substance has the structure R-COH=CCO and like salicylaldehyde and ortho-hydroxyacetophenone it should be expected to have a broad weak OH absorption band extending from 3500 cm^{-1} to beyond 2900 cm^{-1}. However, the absence of any OH-absorption in this region has been reported and is due to the fact that the band is weak and may be superimposed upon the strong CH stretching absorption near 3000 cm^{-1} [60].

The first three compounds in Table 4 have weak maxima between 2720 and 2530 cm^{-1}, which are due to the dimeric form of the carboxylic acids and the C-H stretching vibrations of the aldehyde group.

The carbonyl functions of the substituted benzopyrans listed in Table 3 also follow the rules given by Bellamy. The dimethoxy-benzopyrones have carbonyl absorption bands at 1682 and 1675 cm^{-1}, respectively. Due to conjugate chelation the 5:7-dihydroxy-2:2-dimethyl-chromanone absorbs at a lower frequency and has a strong maximum at 1643 cm^{-1}. The mono-acetate (VIII) has an absorption band at 1745 cm^{-1} coinciding with the standard value for an isolated ester group.

The two carboxylic acids in Table 4 have the maxima due to the carboxyl C=O group conjugated with the benzene ring at 1675 and 1688 cm^{-1}, respectively. The small shift in position may be due to the fact that the mono-acid was measured as a solid and the dicarboxylic acid in chloroform solution. The second acidic group of the dicarboxylic acid (VII) has its absorption maximum at 1735 cm^{-1} ($CHCl_3$ solution), which is 10 cm^{-1} higher than the value given by Bellamy for saturated aliphatic acids measured as solids.

The value obtained for the absorption maximum of the aldehyde group in conjugation with the benzene ring is 1676 cm^{-1}. Aryl aldehydes usually absorb in the range 1715-1695 cm^{-1} in solution, but this value is modified

by the nature and position of ring substituents. Vanillin, 3-methoxy-4-hydroxy-benzaldehyde, also absorbs at 1676 cm^{-1} in chloroform solution[61].

When the infra-red spectra of ageratochromene and its derivatives were studied during the experimental work, a correlation table published by F. A. Miller[62] was consulted. The stretching frequency of the aldehyde group was stated to occur within the range 1730-1675 cm^{-1}. For this reason the 1742 cm^{-1} maximum of (V) originally was not associated with an aldehyde group, but was thought to be the maximum of an isolated aliphatic ester. Bellamy gives the absorption region 1740-1720 cm^{-1} for the saturated aliphatic aldehyde group, and this nearly covers the values 1740 and 1742 cm^{-1} found in Table 4. It is commonly stated that the values given for the solid state are lower than those in solution, but the difference is negligible in this case.

It is known that a halogen substituent at the α-position produces a high-frequency shift of the C=O absorption. Kagarise[63] found a linear relationship between the carbonyl frequency in esters of the type X-COOR and the electronegativity of X, where X represented a methyl group substituted with halogens. One may get an idea of the electronegativity of the phenoxy group which occurs in the compounds (V), (VI) and (VII) (Table 4), by comparing the dissociation constant of phenoxyacetic acid with that of acids substituted with halogen in the α-position. The increase in the dissociation constant by substitution of electronegative atoms such as chlorine in the hydrocarbon chain is attributed to the inductive effect, the effect of the electronegative atom being transmitted through the chain to the oxygen atom, and to the electrostatic interactions[64].

Table 5. Dissociation constants of monocarboxylic acids.

	K_a	Temperature	References
CH_3COOH	$1.75 \cdot 10^{-5}$	25°	65
$PhCH_2CH_2COOH$	$2.29 \cdot 10^{-5}$	"	66
$Ph.CH_2.COOH$	$4.9 \cdot 10^{-5}$	"	66
$Ph.COOH$	$6.3 \cdot 10^{-5}$	"	65
CH_3O-CH_2COOH	$3.35 \cdot 10^{-4}$	"	67
$C_6H_5O-CH_2COOH$	$7.56 \cdot 10^{-4}$		68
$Br.CH_2.COOH$	$1.38 \cdot 10^{-3}$	"	65
$Cl.CH_2.COOH$	$1.4 \cdot 10^{-3}$	"	65
$C_6H_5C \equiv C.COOH$	$5.89 \cdot 10^{-3}$	"	66
$Cl_2CH\ COOH$	$5 \cdot 10^{-2}$	"	65
$Cl_3.C.COOH$	$2 \cdot 10^{-1}$	18°	65

From Table 5 it may be seen that phenoxyacetic acid is a stronger acid than phenylacetic acid and methoxyethanoic acid but only half as strong as monobromo- and monochloroacetic acid. From this fact one may conclude that the electron-attracting power of the phenoxy group has a value between that of methoxyl and bromine. Substitution of an α-bromo group results in an increase in the C=O frequency of about 20 cm^{-1} from the normal position in the infra-red spectrum[69]. Being less electronegative than bromine, the phenoxy grouping of the phenoxyacetaldehyde is expected to cause a smaller displacement. When measured as a liquid, phenoxyacetaldehyde exhibited an infra-red maximum at 1745 cm^{-1} (Figure 17), that is $\Delta\nu = 5$ cm^{-1} higher than the upper limit of the normal absorption. Control measurements of phenoxyacetone showed an infra-red maximum at 1735 cm^{-1}, which was found when the spectrum was measured either on the pure liquid or on a $CHCl_3$ solution (Figure 16). Here the shift is $\Delta\nu = 10$ cm^{-1} above the upper limit of the normal C=O absorption. Therefore, the electronegative value of the phenoxy group may be the reason for the relatively high value of the C=O maximum of the aldehyde Ar-O-C $(CH_3)_2CHO$ (V), (VI) and the acid Ar-O-$C(CH_3)_2COOH$ (VII).

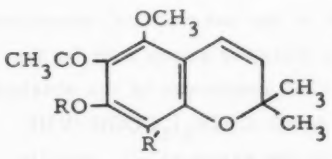
Aryl ethers and other enol ethers with the group =C-O- usually absorb in the region 1270-1230 cm^{-1}, while alkyl ethers absorb in the approximate range 1150-1060 cm^{-1}. In the substituted chromans two

different types of aromatic ethers exist, i.e. the methoxyl and the cyclic ones. In a sixmembered ring where the strain is low, the C-O-C stretching frequency should appear near to the normal value. Bellamy postulates that chain branching at the carbon atom carrying the ether link may modify the C-O- frequency. He has observed also that aralkyl ethers have bands in both the above mentioned regions. Tetrahydropyran have a series of bands in the region 1124-1030 cm^{-1}, and the maximum at 1100 cm^{-1} has been ascribed to the C-O- vibration[70]. But ageratochromene and its derivatives have too many maxima in the region 1300-1000 cm^{-1} to permit a detailed correlation to be made. The compounds in Table 3 have carbonyl and hydroxyl functions which absorb in this region as does the $(CH_3)_2C$ group. In general, the spectra are so complex that it has not been possible to find any maxima which are characteristic of the chroman ring.

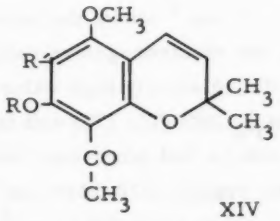
7. 2:2-DIMETHYL-CHROMENE DERIVATIVES IN NATURE

A number of substituted 2:2-dimethyl-chromenes occur in natural products. In Chemical Abstracts these compounds are listed as derivatives of 2H-1-benzopyran.

The leaves of the Australian trees Evodia elleryana, Evodia littoralis and Medicosma cunninghamii Hook have been investigated, and the chromenes found are listed in Table 6. The evodionol- and alloevodionol series are based on formula (XIII) and (XIV) respectively.



XIII



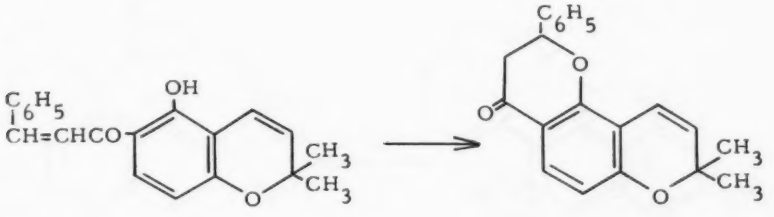
XIV

Table 6

	Evodionol series (XIII)	Alloevodionol series (XIV)
R=R'=H	Evodionol[71,72] from Evodia littoralis	Alloevodionol[73] from Medicosma cunninghamii
$R=CH_3$ $R'=H$	Methyl-evodionol[73] from Medicosma cunninghamii	Methyl-alloevodionol[73,74] found in Evodia elleryana (from Mackay districts only)
$R=CH_3$ $R'=OCH_3$	Evodione[24,74] found in Evodia elleryana (from Stradbroke Island only)	Alloevodione[75] from Evodia elleryana.

Evodionol and methyl-alloevodionol have been found also in the bark of Melicope simplex grown in New Zealand[76].

By ether extraction of the seeds and roots of Lonchocarpus sericeus from the Belgian Congo, lonchocarpine was obtained[77]. The substance formed yellow-orange crystals. It has the formula (XV). Cyclization resulted in the formation of the corresponding flavanone (XVI).

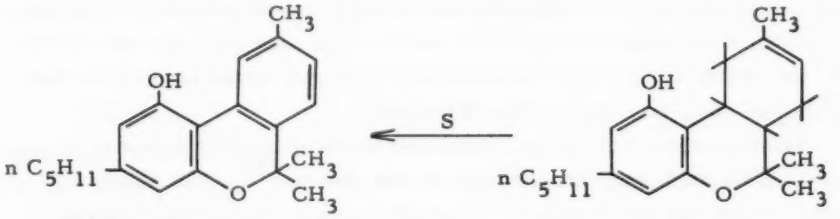


XV Lonchocarpine XVI

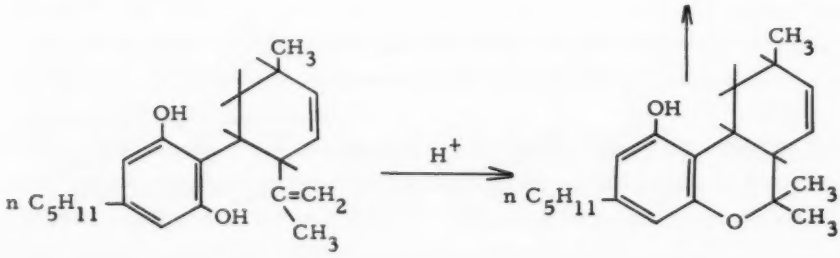
The hemp plant, Cannabis sativa L., now is cultivated in many parts of the temperate zone; its native habitat seems to be Asia Minor[78]. The long bast fibers of its stem are utilized for making cordage and certain coarser cloths. The tops of the plants and a resinous product obtained from them have been used for about two thousand years in India, Persia and other parts of the East as intoxicating agent. In Mexico, Latin America and the United States the narcotic has been employed under the name marihuana. Among many other names for the drug we find the Arabian hashish and the Persian beng[79].

Cannabinol (XVII) was isolated as its acetate from the resin of Cannabis sativa L. in 1898 by Dunstan and Henry[80] and in 1899 by Wood, Spivey and Easterfield[81]. About forty years later Jacob and Todd[82] isolated the same substance together with cannabidiol (XVIII) from a fresh sample of the Egyptian drug. Adams et al.[83, 84] determined the structures of the two substances which were obtained from the red oil of Minnesota wild hemp. The position of the cyclic double bond in (XVIII), although probably correct, has not been rigidly established.

(XVII) and (XVIII) possess only slight marihuana activity, but cannabidiol can be isomerized to a highly active tetrahydrocannabinol[85,84] (XIX). Wollner et al.[86] isolated a tetrahydrocannabinol with high



XVII Cannabinol XIX

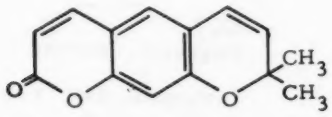


XVIII Cannabidiol XIX

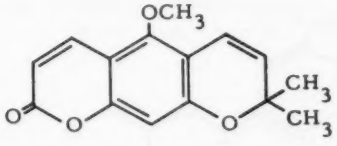
activity from marihuana. It was isomeric with, but different from those prepared by Adams. Levine[87] has concluded that cannabinol is formed in cannabis by the spontaneous dehydrogenation of tetrahydro-cannabinol.

A special group of substances with a 2:2-dimethylchromene structure is the coumarino-chromenes. From the bark of Zanthoxylum americanum Mill. three representatives of this group were isolated. They are xanthyletin (XX), its 5-methoxy-derivative xanthoxyletin (XXI) and allo-xanthoxyletin (XXII). Alexander Robertson and collaborators[88, 16, 89] elucidated

their structures. From the bark of Halfordia scleroxyla Hegarty and Lahey[90] also isolated xanthoxyletin, and the same substance together with xanthyletin was found in East Indian satinwood, Chloroxylon swietenia, by King et al.[91].



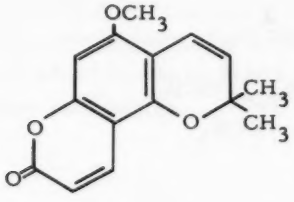
XX Xanthyletin



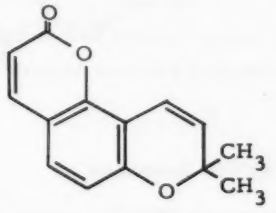
XXI Xanthoxyletin

Seselin has been found in Seseli indicum (Wall.) W. et A. and in Skimmia japonica Thbg., and the structure (XXIII) was put forward by Späth et al.[92]. A team from the same institute elucidated the structure of luvangetin (XXIV) which was isolated together with xanthyletin, from the roots and fruits of the Bengalese plant Luvunga scandens Ham.[93].

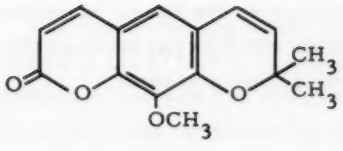
By light petroleum extraction of the bark of the Australian Flindersia brayleyana braylin (XXV) was obtained[94]. (XXV) is a methoxy derivative of seselin.



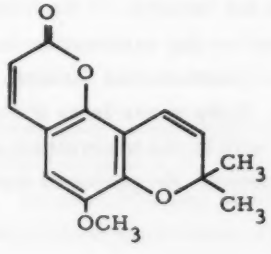
XXII Allo-xanthoxyletin



XXIII Seselin

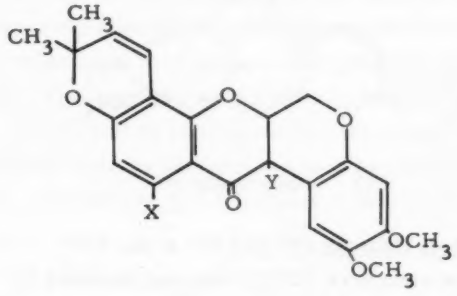


XXIV Luvangetin



XXV Braylin

The 2:2-dimethyl-benzopyran forms part of many other natural products which are more complicated. The insecticides deguelin, tephrosil and toxicarol (XXVI) from the derris root are among the best known.

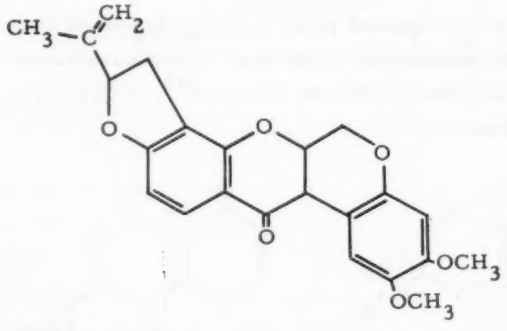


XXVI
Deguelin , X=Y=H

Tephrosil , X=H Y=OH

Toxicarol , X=OH Y=H

The most important insecticide and fish poison found in the same

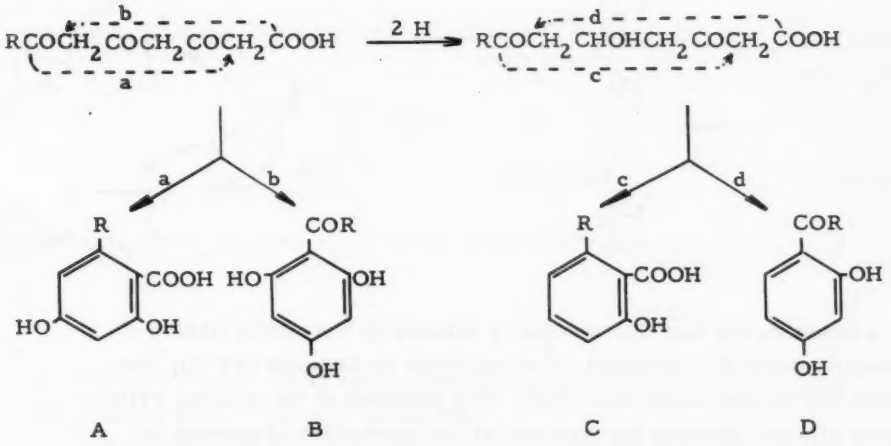


XXVII Rotenone

plant is rotenone (XXVII), which instead of the pyran ring has a dihydrofuran ring.

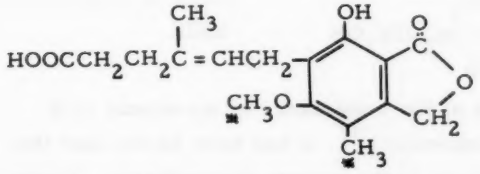
At about the beginning of this century Collie (for ref. see Birch[95]) published his theories of the biosynthesis of phenolic substances. They were based on the assumption that acetic acid molecules were linked together in a head-to-tail fashion, and known types of cyclization reactions followed. Fifty years later Birch[95], inspired by the known importance of acetic acid in the biosynthesis of steroids and fats put forward the same theories. He proposed the following reaction scheme:

$$RCOOH + CH_3COOH + CH_3COOH + CH_3COOH \longrightarrow$$



RCOOH may be a fatty acid.

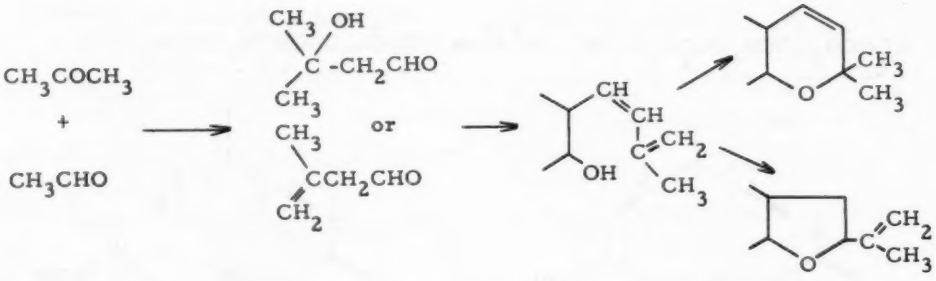
A methyl group may be introduced by means of methionine, as demonstrated by Birch et al.[96] in the case of mycophenolic acid (XXVIII) from Penicillium brevi-compactum. By feeding (methyl-^{14}C) methionine to P. brevi-compactum, followed by degradation studies of the mycophenolic acid which had been produced, the groups marked with an asterisk were found radioactive.



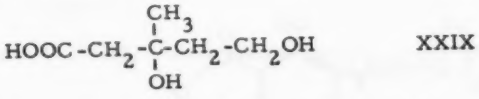
XXVIII
Mycophenolic acid

The evodionol and alloevodionol series may be derived from the compound B (p. 47) by methylation and attachment of a C_5 residue. Alexander Robertson and collaborators[45] assume that this attachment is one of the final processes in the phytochemical production of the 2:2-

dimethyl-benzopyran and dihydro-benzofuran series. They suggest the following route:



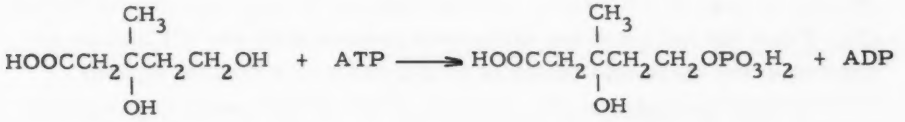
It is based on the fact that acetone is formed by hydrolytic fission of certain natural 2:2-dimethyl-Δ^3-chromenes as deguelin (XXVI), toxicarol (XXVI) and xanthyletin (XX). The reversal of the scheme written above offers a feasible mechanism for the production of acetone by hydrolytic cleavage. Rotenone (XXVII) and deguelin (XXVI) are only two among many examples of the occurrence of a 2:2-dimethyl-Δ^3-chromene and an isomeric coumaran system in the same or closely related plant species. This fact, too, makes it reasonable to assume that both types originate from the same intermediate. Cannabidiol (XVIII) and cannabinol (XVII) are both found in marihuana, and (XVII) is supposed to be formed from (XVIII) by a cyclization in the manner mentioned above followed by a dehydrogenation.

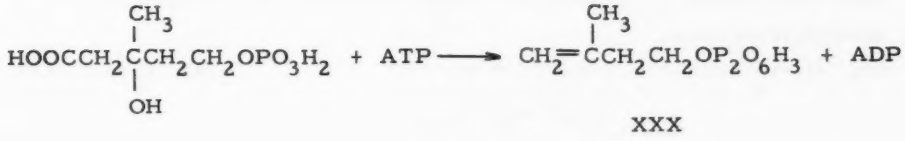


XXIX

Through the investigations of the importance of mevalonic acid (XXIX) by Karl Folkers and collaborators[97], it has been shown that this substance is a specific intermediate in the terpene biosynthesis. Lynen et al.[98] simultaneously with K. Bloch and collaborators, found isopentenyl-pyrophosphate (XXX) to be an intermediate in the biological synthesis of squalene from mevalonic acid. With liver enzymes synthetic ^{14}C-isopentenyl-pyrophosphate in a short time gave a radioactive cholesterol, and by incubation with latex from Taraxacum Kok saghuz radioactive

rubber was formed. Therefore (XXX) is believed to be the biological isoprene unit.





XXX

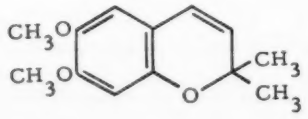
A reaction between (XXX) and a phenolic compound followed by a dehydrogenation then will give a chromene.

The aromatic ring of ageratochromene may be formed from three acetate units. Attaching a C_5 residue to this ring will produce a 5:7-dihydroxy-2:2-dimethylchromene. Shikimic acid, itself derived from glucose, may also be the precursor of the aromatic ring. Introduction of further hydroxyl groups or removal of these groups should present no biological difficulties; many enzymes connected with these reactions are at present known in animal tissues[99]. Therefore, the formation of 6:7-dihydroxy-2:2-dimethylchromene and subsequent methylation to the corresponding dimethoxy compound (ageratochromene) biologically should be quite possible.

SUMMARY

Ageratum houstonianum Mill. with the synonym Ageratum mexicanum Sims belongs to the family Compositae. From the essential oil of this plant a crystalline substance $C_{13}H_{16}O_3$ (I) with m.p. 47.5° was obtained. The name ageratochromene was proposed for it. The oxidations

which were carried out to degrade (I) to a substance with a smaller number of C-atoms in order to determine its structure, are illustrated in the scheme on page 11. Catalytic hydrogenation of (I) gave a dihydrocompound (II). From the infra-red and ultraviolet spectra of (I) and (II) it could be concluded that the double bond was conjugated with a benzene nucleus. Based on the knowledge of the structure of (I) obtained during the experimental work, 6:7-dimethoxy-2:2-dimethyl-chroman (X) was synthesized, and (X) was identical with (II) according to melting point, mixed melting point and infra-red spectrum. Ageratochromene is therefore 6:7-dimethoxy-2:2-dimethylchromene.



I

After the experimental part of this work was finished, R. Huls[18] synthesized 6:7-dimethoxy-2:2-dimethyl-chromene, which had the same melting point and ultraviolet maxima as ageratochromene (compare Table 1, p. 10

The infra-red spectra of nine chroman derivatives and of four 1:2:4:5-substituted benzene derivatives obtained during the experimental work, are discussed. Some simple 2:2-dimethyl-chromenes occurring in Nature are discussed in relation to the theories of Birch[95] and Lynen[98] in order to put forward a hypothesis for the possible biochemical synthesis of ageratochromene.

ACKNOWLEDGMENTS

The experimental part of this work was carried out at the Institute for Organic Chemistry, The Technical University of Norway, during the years 1952-1955. To the head of the institute, Professor Nils Andreas Sørensen, I would like to express my most sincere thanks for guidance throughout the work.

My thanks are also due to Dr. Torger Bruun, who has carried out most of the semi-microanalyses.

REFERENCES:

1 Engler, A. : Syllabus der Pflanzenfamilie, 11th Ed., Gebrüder Borntraeger, Berlin, 1936, p. 368.

2 Marzell, H. : Wörterbuch der Deutschen Pflanzennamen, Vol. I, S.Hirzel, Leipzig, 1943, p. 138.

3 Gerth van Wijk, H.L. : A Dictionary of Plantnames, Vol. I, Martinus Nijhoff, The Hague, 1911, p.44.

4 Lange, J. : Plantenavne, Håndbogserie Nr. 24, Alm. Dansk Gartnerforening, København, 1949, p. 12.

5 Thorsrud, A. and Reisæter, O. : Norske Plantenavn, Meldinger fra Norges Landbrukshøgskole, Vol. 28, Nr. 1-4, Oslo, 1948, p. 4.

6 Daydon Jackson, D. : Index Kewensis, Part I, Clarendon Press, Oxford, 1893.

7 Jenssen, J. : Ordbog for Gartnere og Botanikere, 4th Ed., G.E.C. Gads Forlag, København, 1946, p.7, 151, 118.

8 Chevalier, J. : Bul.gén. Ther. 159(1910) 466.

9 Wehmer, C. and Hadders, M. : in Klein, G., Handbuch der Pflanzenanalyse, Vol. IV, Julius Springer, Wien, 1933, p. 793.

10 Molisch, H. and Zeisel, S. : Ber.deut.botan. Ges. 6(1888) 353.

11 Moudgill, Kishori Lai : Quart. J. Indian Chem. Soc. I(1925) 273. C.A. 19(1925) 2388.

12 Joly, L. : Parfumerie mod. 31(1937) 25. C.A. 31(1937) 2750.

13 Biquard, D. : Bull.soc.chim. France. 8(1941) 55.

14 Wegscheider, R. : Monatsch. Chem. 16(1895) 75, p. 81.

15 Thompson, H.W. and Torkington, P. : J. Chem. Soc. 1945 640.

16 Robertson, A. and Subramaniam, T.S. : J. Chem. Soc. 1937 286.

17 Alertsen, A. Rye : Acta Chem. Scand. 9(1955) 1725.

18 Huls, R. : Bull. Soc. Chim. Belg. 67(1958) 22.

19 Mancera, O., Barton, D.H.R., Rosenkranz, G. and Djerassi, C.: J. Chem. Soc. 1952 1021, p. 1025.

20 Lahey, F. N. : Univ.Queensland Papers, Dept. Chem. I(1940) No. 17.

21 Pregl, F. : Quantitative Organische Mikroanalyse (neubearbeitet von H. Roth), 6th Ed., Springer Verlag, Wien, 1949, p.106.

22 Vogel, A. J. : A Textbook of Practical Organic Chemistry Including Qualitative Organic Analysis, 3rd Ed., Longmans, Green and Co., London, 1956, p. 289.

23 Heyes, R. G. and Robertson, A: J. Chem. Soc. 1935 681 p. 684.

24 Wright, S. E. : J. Chem. Soc. 1948 2005.

25 Pregl, F. : Ref. 21, p. 226.

26 Criegee, R., Marchand, B. and Wannowius, H. : Ann. 550 (1942) 99.

27 Fieser, L.F. : Experiments in Organic Chemistry, 2nd Ed., D.C. Heath and Company, Boston, 1941, p. 436.

28 Meyer, H. : Analyse und Konstitutionsermittlung Organischer Verbindungen, J. Springer, Wien, 1938, p. 520.

29 Waters, W.A. : in Gilman, H., Organic Chemistry, Vol.IV, John Wiley & Sons, New York, 1953, p. 1211.

30 Shirley, D.A. : Preparation of Organic Intermediates, John Wiley & Sons, New York, 1951, p. 247.

31 Blatt, A. H. : Org. Syn. Coll. Vol. II 1944 88.

32 Whitney, W. B. and Henze, H. R.: : J. Am. Chem. Soc. 60(1938) 1148.

33 Gilman, H. and Blatt, A.H. : Org.Syn. Coll. Vol. I, 2nd. Ed., 1944 296.

34 Lange, N.A. : Handbook of Chemistry, 5th Ed., Handbook Publishers, Inc., Sandusky, Ohio, 1944, p. 495.

35 Speer, R.I. and Mahler, H.R. : J.Am.Chem.Soc. 71(1949) 1133.

36 Hatch, L.F. and Nesbitt, S.S. : J.Am.Chem.Soc. 67(1945) 39.

37 Wegscheider, R. : Monatsh. Chem. 3(1882) 348.

38 Wegscheider, R. and Späth, E. : Monatsh.Chem. 37(1916) 277 p. 282.

39 Rodionow, W.M., Kanewskaja, S.J. and Kupinskaja, G.W. : Ber. 62(1929) 2563.

40 Windaus, A. and Hermanns, L.: Ber. 47(1914) 1470.

41 Goldschmiedt, G. : Monatsh. Chem. 9(1888) 762.

42 Gilman, H. and Blatt, A.H. : Org.Syn.Coll. Vol. I, 2nd. Ed., 1944 250.

43 Hodgman, C.D. : Handbook of Chemistry and Physics, 39th Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1957-1958, p. 1028.

44 Blatt, A.H. : Org.Syn. Coll. Vol. II 1944 93.

45 Bridge, W., Heyes, R.G. and Robertson, A. : J.Chem.Soc. 1937 279.

46 Fieser, L.F. : Ref. 27, p. 381.

47 Barton, D.H.R., Fawcett, J.S. and Thomas, B.R. : J.Chem.Soc. 1951 3147 p.3154.

48 Blatt, A.H. : Org.Syn.Coll. Vol. II 1944 622.

49 Blatt, A.H. : Org.Syn.Coll. Vol. II 1944 44.

50 Birch, H.F., Robertson, A. and Subramaniam, T.S. : J.Chem. Soc. 1936 1832.

51 Richards, J.H., Robertson, A. and Ward, I. : J.Chem. Soc. 1948 1610.

52 Bellamy, L.J. : The Infra-red Spectra of Complex Molecules, Methuen & Co., London, 1956, p. 119.

53 Bellamy, L.J., Hallam, H.E. and Williams, R.L. : Trans. Faraday Soc. 54 (1958) 1120.

54 Bellamy, L.J. and Williams, R.L. : Trans. Faraday Soc. 55 (1959) 14.

55 Bellamy, L.J. : Ref. 52, p. 14.

56 Thompson, H.W. and Torkington, P. : Proc.Roy. Soc. A 184 (1945) 3.

57 Bellamy, L.J. : Ref. 52, p. 24.

58 Bellamy, L.J. : Ref. 52, p. 60.

59 Dannenberg, H., Schiedt, V. and Steidle, W. : Z. Naturforsch. 8B (1953) 269.

60 Bellamy, L.J. : Ref. 52, p. 91.

61 Bellamy, L.J. : Ref. 52, p. 134.

62 Miller, F.A. : in Gilman, H. Organic Chemistry, Vol. III, John Wiley & Sons, New York, 1953, p. 146.

63 Kagarise, R.E. : J.Am.Chem.Soc. 77 (1955) 1377.

64 Pauling, L. : The Nature of the Chemical Bond, Cornell University Press, Ithaca, N.Y., 1945, p. 204.

65 Hodgman, C.D. : Ref. 43, p. 1644.

66 Fieser, L.F. and Fieser, M. : Organic Chemistry, 2nd Ed., D.C. Heath and Company, Boston, 1950, p. 708.

67 Ostwald, W. : Z.physik. Chem. Leipzig. 3 (1889) 170.

68 Behaghel, O. : J.prakt. Chem. 2 114 (1926) 287.

69 Bellamy, L.J. : Ref. 52, p. 121.

70 Bellamy, L.J. : Ref. 52, p. 104.

71 Lahey, F.N. and Jones, T.G.H. : Univ.Queensland Papers, Dept. Chem. I (1939) No.13.

72 Lahey, F. N. : Univ.Queensland Papers, Dept. Chem. I (1942) No. 20.

73 Sutherland, M.D. : Univ.Queensland Papers, Dept. Chem. I (1949) No. 35.

74 Jones, T.G.H. and Wright, S.E. : Univ.Queensland Papers, Dept. Chem. I (1946) No. 27.

75 Kirkby, K.D. and Sutherland, M.D. : Australian J. Chem. 9 (1956) 411.

76 Briggs, L.H. and Locker, R. H. : J. Chem. Soc. 1950 2376.

77 Baudrenghien, J., Jadot, J. and Huls, R. : Bull.classe sci., Acad.roy. Belg. 39 (1953) 105.

78 Osol, A. and Farrar, G.E. : The Dispensatory of the United States of America, 25th Ed., L.B. Lippincott Company, Philadelphia, 1957, p. 1613.

79 Kropa, E.L. : Battelle Tech.Rev. 7(1958) No.6 p.9.

80 Dunstan, W.R. and Henry, T.A. : Proc.Chem.Soc. 1898 44.

81 Wood, T.B., Spivey, W.T.N. and Easterfield, T.H. : J.Chem.Soc. 75(1899) 20.

82 Jacob, A. and Todd, A.R. : Nature 145(1940) 350.

83 Adams, R., Baker, B.R. and Wearn, R.B. : J.Am.Chem.Soc. 62(1940) 2204.

84 Adams, R., Loewe, S., Pease, D.C., Cain, C.K., Wearn, R. B., Baker, B.R. and Wolff, H. : J.Am.Chem.Soc. 62(1940) 2566.

85 Adams, R., Pease, D.C., Cain, C.K. and Clark, J.H. : J.Am.Chem.Soc. 62(1940) 2402.

86 Wollner, H.J., Matchett, J. R., Levine, J. and Loewe, S. : J.Am.Chem.Soc. 64(1942) 26.

87 Levine, J. : J.Am.Chem.Soc. 66(1944) 1868.

88 Bell, J.C. and Robertson, A. : J.Chem.Soc. 1936 1828.

89 Robertson, A. and Subramaniam, T.S. : J.Chem.Soc. 1937 1545.

90 Hegarty, M.P. and Lahey, F.N. : Australian J. Chem. 9(1956) 120.

91 King, F.E., Housley, J.R. and King, T.J. : J.Chem.Soc. 1954 1392.

92 Späth, E., Bose, P.K., Matzke, J. and Guha, N.C. : Ber. 72(1939) 821.

93 Späth, E., Bose, P.K., Schmid, H., Dobrovolny, E. and Mookerjee, A. : Ber. 73B(1940) 1361.

94 Anet, F.A.L., Hughes, G.K. and Ritchie, E. : Australian J.Sci.Research. 2A(1949) 608.

95 Birch, A.J. : in Todd, A., Perspectives in Organic Chemistry, Interscience Publishers, Inc., New York, 1956, p. 148.

96 Birch, A.J., English, R.J., Massy-Westrop, R.A., Slaytor, M. and Smith, H. : J.Chem.Soc. 1958 365.

97 Wolf, D.E., Hoffman, C.H., Aldrich, P.E., Skeggs, H.R., Wright, L.D. and Folkers, K. : J.Am.Chem.Soc. 78(1956) 4499.

98 Lynen, F., Eggerer, H., Henning, U. and Kessel, I. : Ang.Chem. 70(1958) 738.

99 Scheline, R.R., Williams, R.T. and Wit, J.G. : Nature 188(1960) 849.

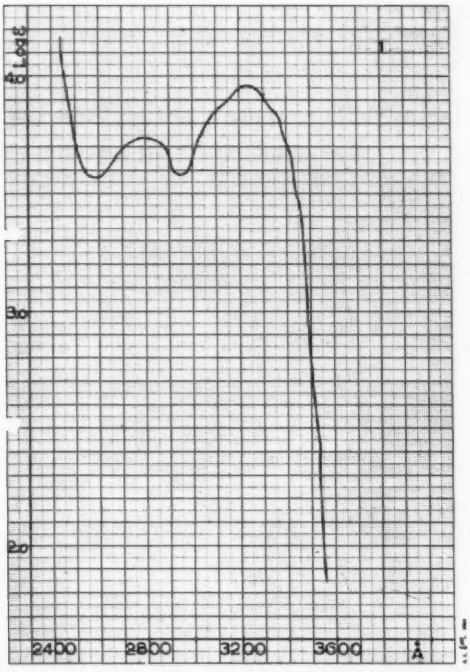


Fig.I. Ultraviolet absorption of ageratochromene in hexane.

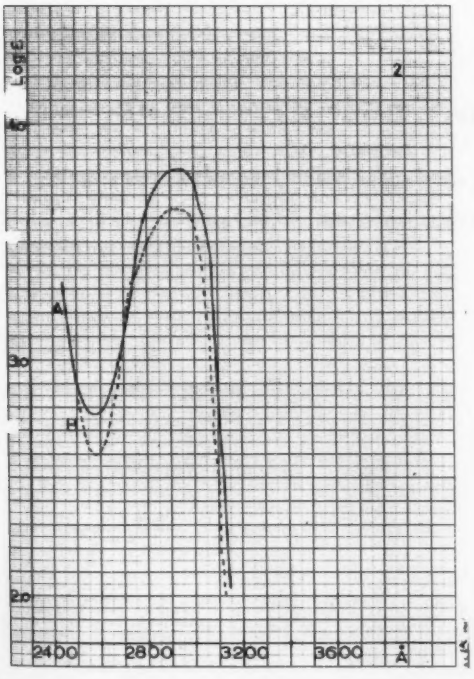


Fig.2. Ultraviolet absorption in hexane of:
A:——3:4-dihydro-ageratochromene (II),
B:---3:4-dihydroxy-ageratochromene (III).

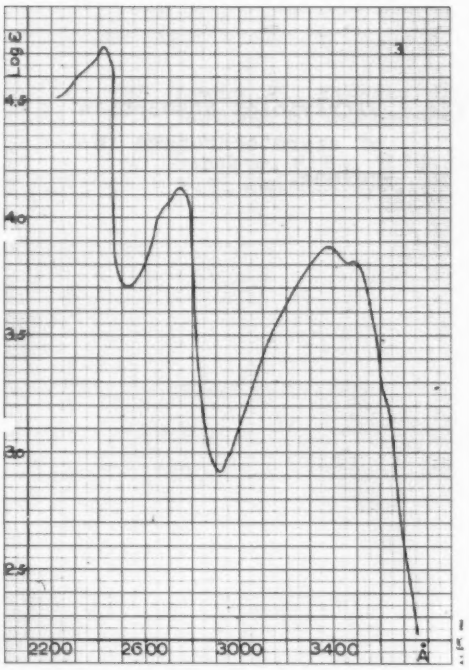


Fig.3. Ultraviolet absorption of compound (IV) in hexane.

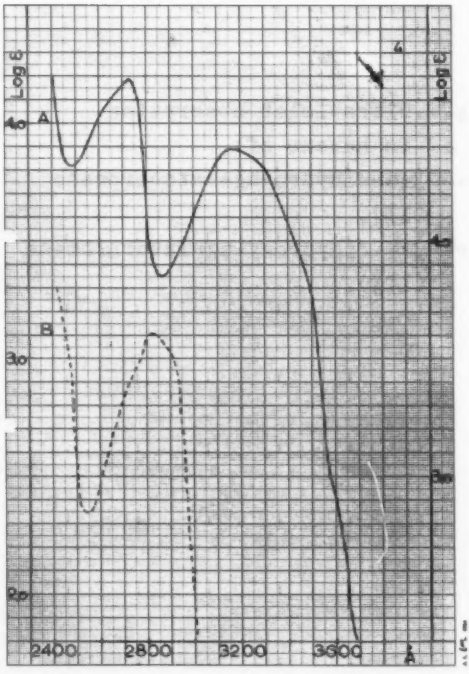


Fig.4. Ultraviolet absorption in hexane of:
A: — compound (V), scale left side,
B: --- compound (XII), scale right side.

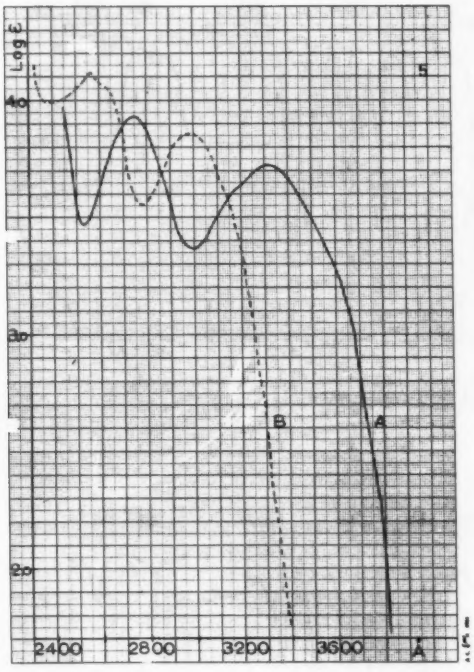


Fig.5. Ultraviolet absorption in ethanol of:
A: —— the monocarboxylic acid (VI)
B: --- the dicarboxylic acid (VII)

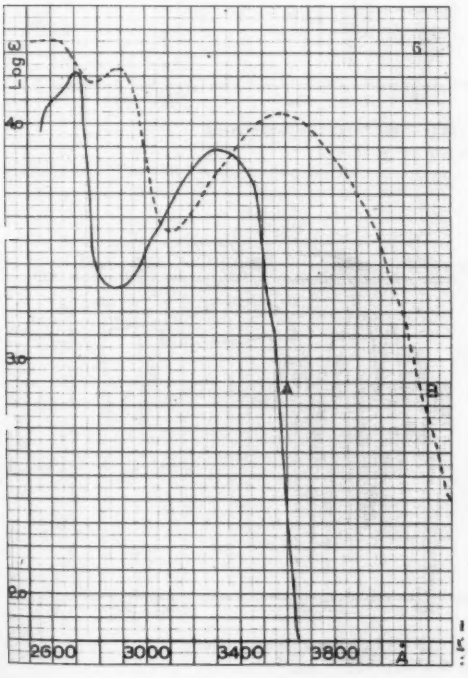


Fig.6. Ultraviolet absorption in hexane of:
A: —— 6:7-dimethoxy-2:2-dimethyl-chromanone,
B: --- 2-hydroxy-4:5-dimethoxy-ω-isopropylidene-acetophenone.

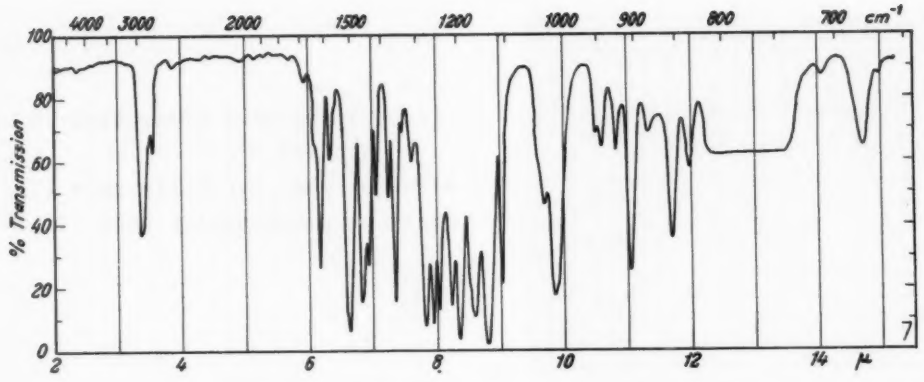


Fig.7. Infra-red absorption of ageratochromene (I) in CCl_4, l=0.05 mm.

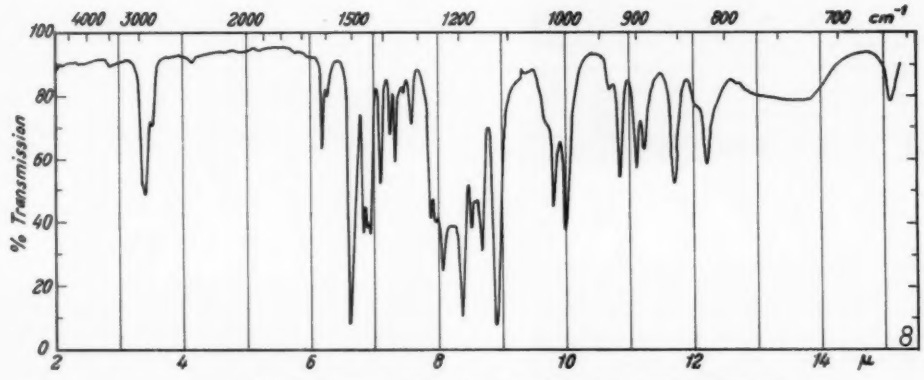


Fig.8. Infra-red absorption of 3:4-dihydro-ageratochromene (II) in $CHCl_3$, l=0.05 mm.

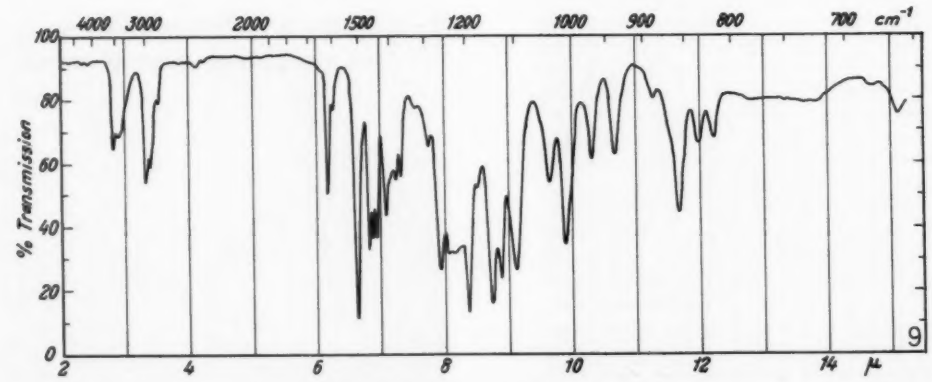


Fig.9. Infra-red absorption of 3:4-dihydroxy-ageratochromene (III) in $CHCl_3$, c=9 mg in 0.1 ml, l=0.05 mm.

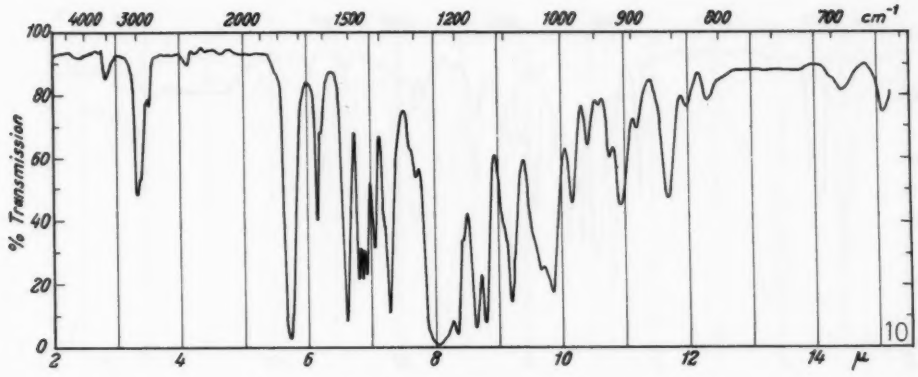


Fig.I0. Infra-red absorption of the monoacetate of compound (III) in $CHCl_3$, l=0.05 mm.

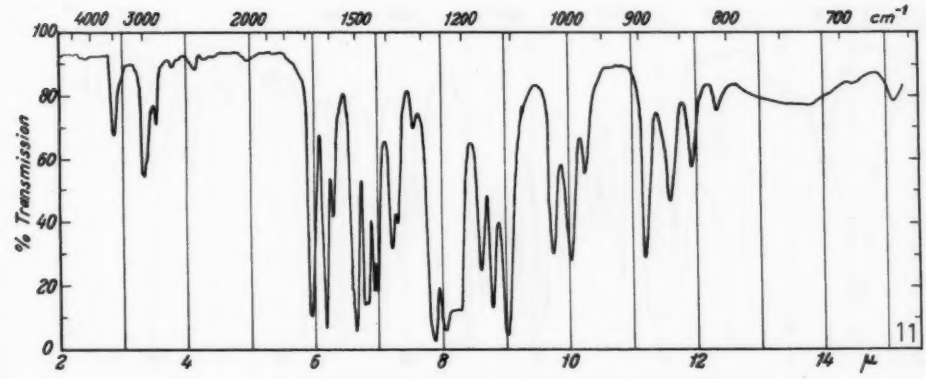


Fig.II. Infra-red absorption of compound (IV) in $CHCl_3$, c=9.3 mg in 0.09 ml, l=0.05 mm.

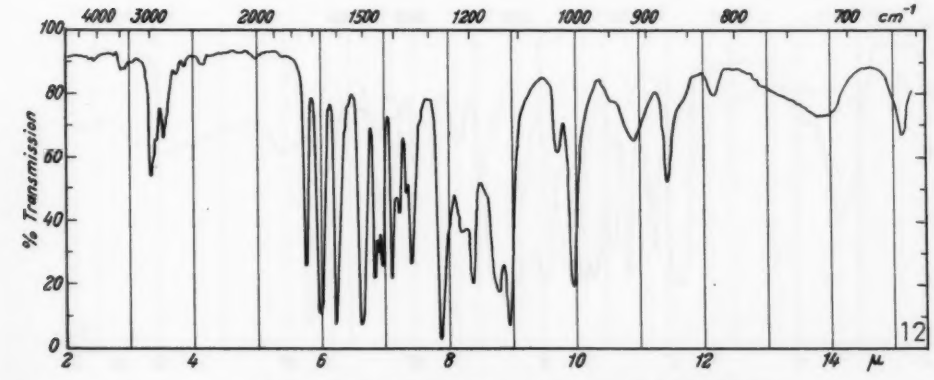


Fig.I2. Infra-red absorption of compound (V) in $CHCl_3$.

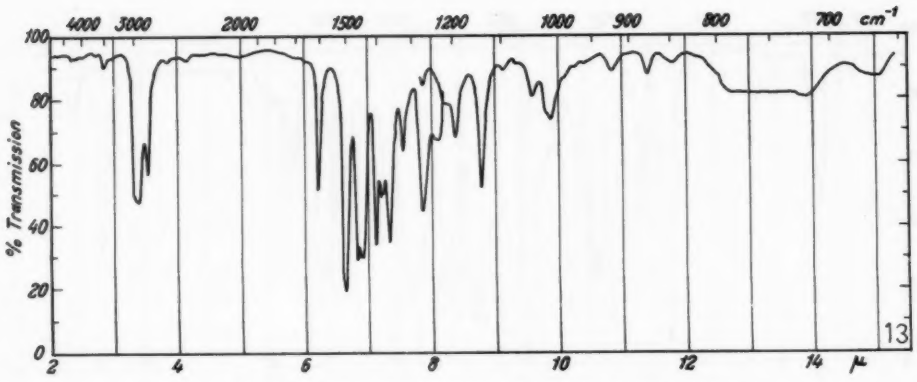


Fig.I3. Infra-red absorption of compound (XII) in $CHCl_3$, l=0.05 mm. At I225 cm^{-I} a dilution had to be made.

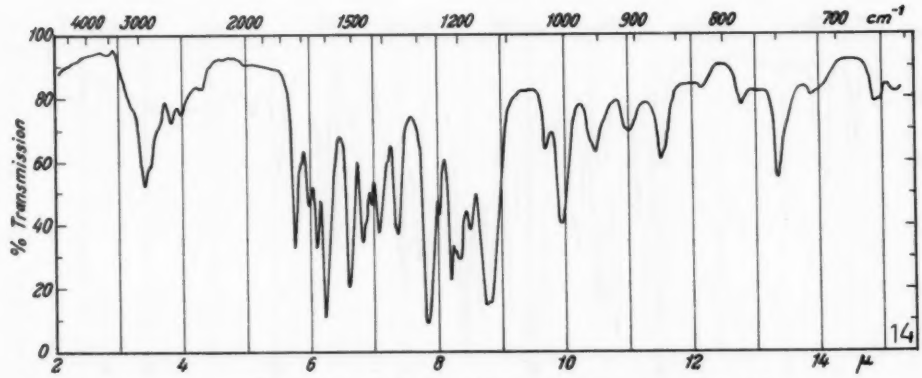


Fig.I4. Infra-red absorption of the monocarboxylic acid (VI) in KBr, c=2.2 mg in 2 g KBr, l=ca.2 mm.

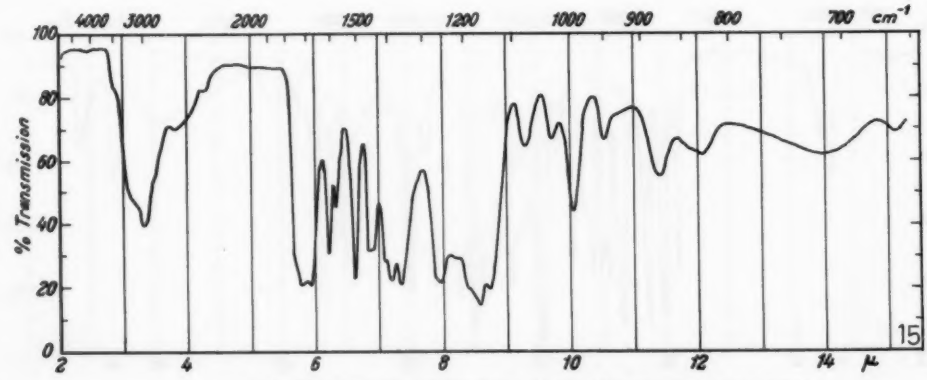


Fig.I5. Infra-red absorption of the dicarboxylic acid (VII) in $CHCl_3$, c=9.5 mg in 0.09 ml, l=0.05 mm.

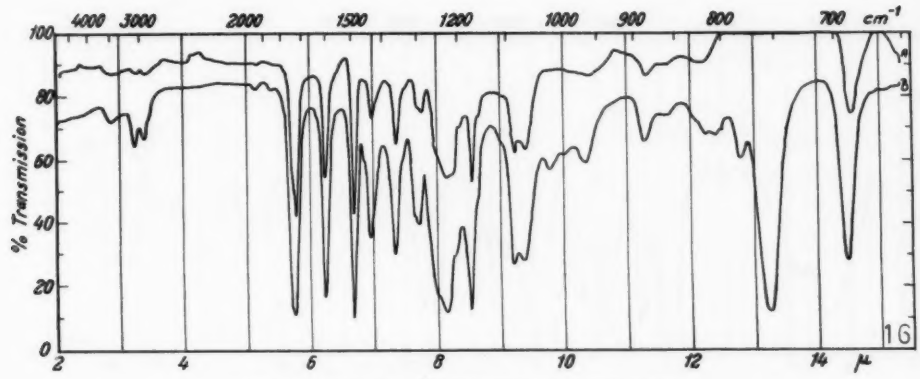


Fig.I6. Infra-red absorption of phenoxyacetone.
A: in $CHCl_3$, c=I5 mg in 0.25 ml, l=0.05 mm.
B: liq.

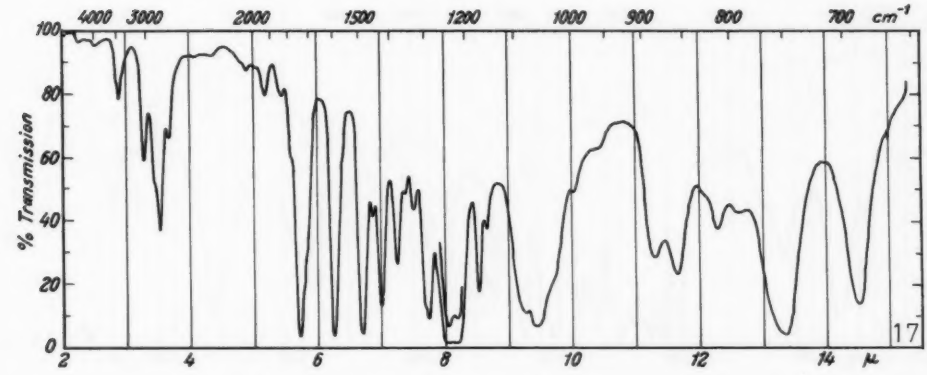


Fig.I7. Infra-red absorption of phenoxyacetaldehyde, liq.

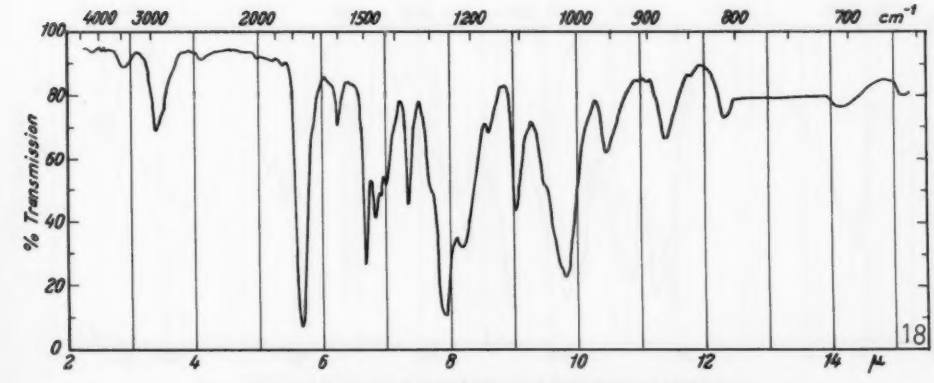


Fig.I8. Infra-red absorption of meconin in $CHCl_3$,
c=II.5 mg in 0.I ml, l=0.05 mm.

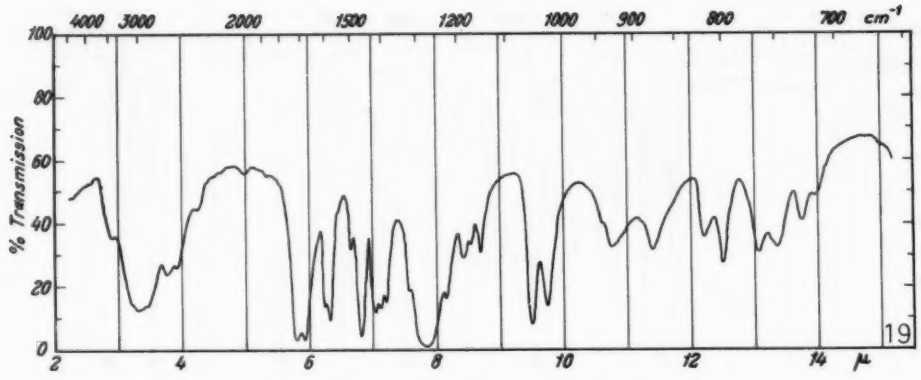


Fig.I9. Infra-red absorption of hemipinic acid in KBr, c=3.9 mg in 2 g KBr, l=ca.2 mm.

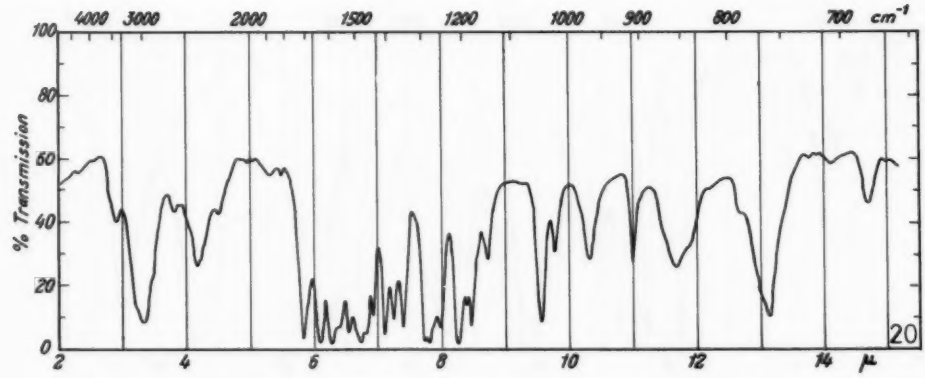


Fig.2o. Infra-red absorption of m-hemipinic acid in KBr, c=4 mg in 2 g KBr, l=ca.2 mm.

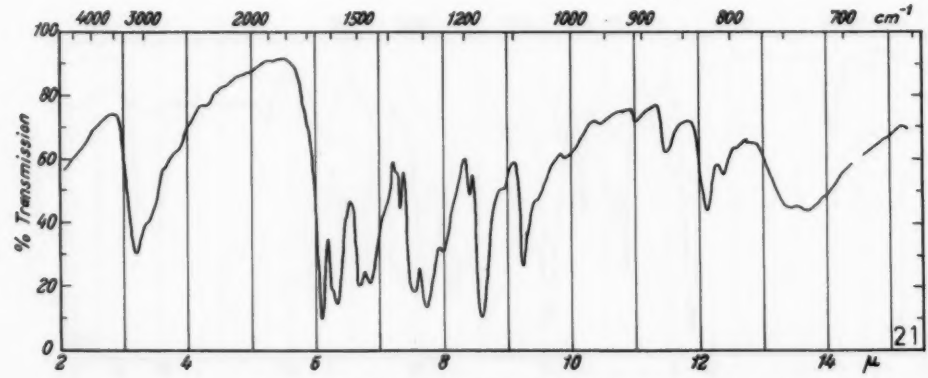


Fig.2I. Infra-red absorption of 5:7-dihydroxy-2:2-dimethyl-chromanone in KBr, c=2 mg in 2 g KBr, l=ca. 2 mm.

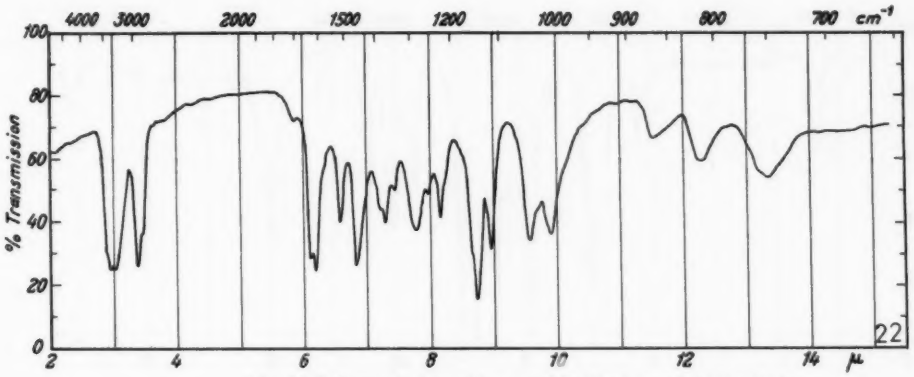


Fig.22. Infra-red absorption of 5:7-dihydroxy-2:2-dimethyl-chroman in KBr, c=I.6 mg in 2 g KBr, l=ca.2 mm.

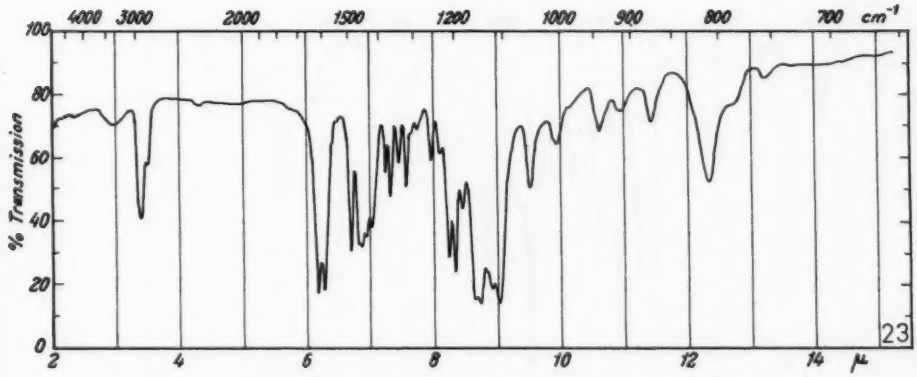


Fig.23. Infra-red absorption of 5:7-dimethoxy-2:2-dimethyl-chroman (IX), liq.

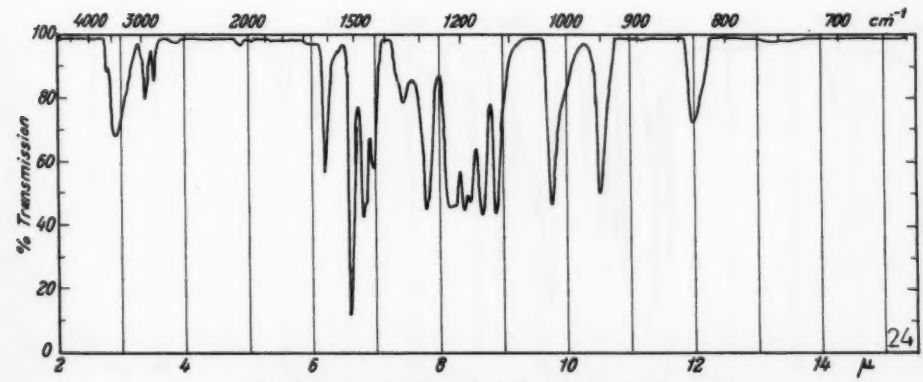


Fig.24. Infra-red absorption of 3:4-dimethoxy-phenol in $CHCl_3$, c=I0.7 mg in 0.I ml, l=0.05 mm.

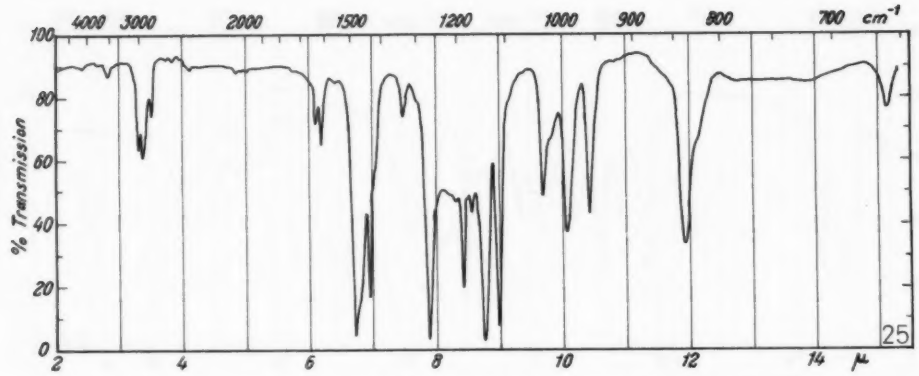


Fig.25. Infra-red absorption of a compound with m.p. 156-157.5 (p.30) in $CHCl_3$, c=10 mg in 0.1 ml, l=0.05 mm.

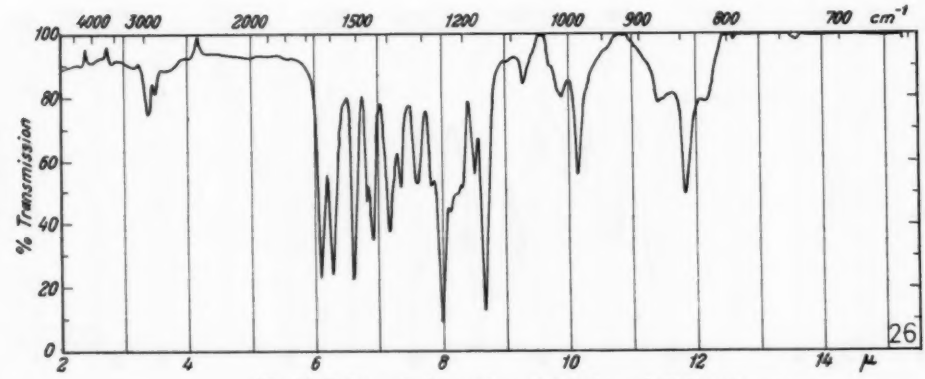


Fig.26. Infra-red absorption of 2-hydroxy-4:5-dimethoxy-ω-isopropylidene-acetophenone in $CHCl_3$, c=10 mg in 0.1 ml, l=0.05 mm.

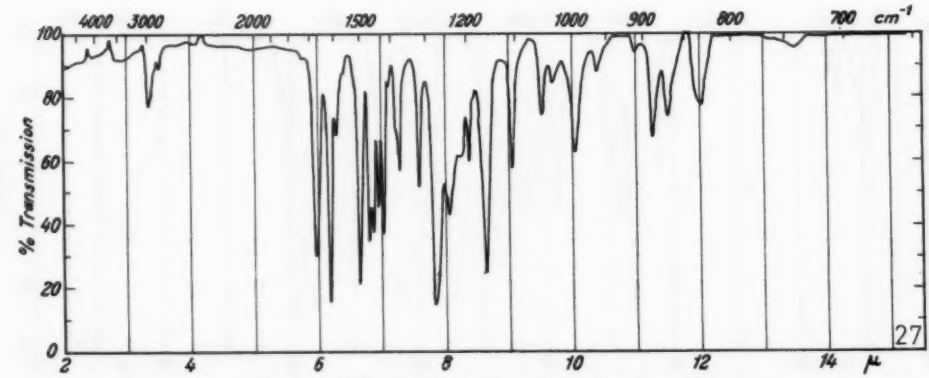


Fig.27. Infra-red absorption of 6:7-dimethoxy-2:2-dimethyl-chromanone in $CHCl_3$, c=10 mg in 0.1 ml, l=0.05 mm.

THE LAST VOLUMES OF ACTA POLYTECHNICA

Chemistry including Metallurgy Series

(The predecessor of Acta Polytechnica Scandinavica)

Volume 4

Nr 9 SANDFORD, F, and FRANSSON, S: *The Refractoriness of Some Types of Quartz and Quartzite.* II. Acta P 173 (1955), 24 pp, Sw. Kr 5: 00 UDC 666.76:549.514.51

Nr 10 BJÖRKMAN, L, BJÖRKMAN, M, BRESKY, A, ENEBO, L, and RENNERFELT, J: *Experiments on the Culture of Chlorella for Food Purposes.* Acta P 176 (1955), 18 pp, Sw. Kr 4: 00 UDC 663.11:582.2

Nr 11 WRANGLÉN, G: *Dendrites and Growth Layers in the Electrocrystallization of Metals.* Acta P 182 (1955), 42 pp, Sw. Kr 6: 50 UDC 669.017:548.232.4:669.017:548.52

Nr 12 MATTSSON, E: *The Electrode Process in Metal Deposition from Aqueous Solutions.* Acta P 184 (1955), 56 pp, Sw. Kr 6: 50 UDC 541.135:621.357

Nr 13 EDHBORG, A: *Studies on a Water-Soluble Material from the Masonite Process.* Acta P 197 (1956), 87 pp, Sw. Kr 12: 50 UDC 547.454:542.938:542.941
out of print

ACTA POLYTECHNICA SCANDINAVICA

Chemistry including Metallurgy Series

Ch 1 JART, A: *Fat Rancidity. Summaries of Papers Presented at the 2nd Scandinavian Symposium on Fat Rancidity.* (Acta P 242/1958) 72 pp, Sw. Kr 7: 00 UDC 665.112.2

Ch 2 ERÄMETSÄ, O: *Ion Characteristics; a New Way of Assessing the Chemical Properties of Ions.* (Acta P 249/1958) 22 pp, Sw. Kr 7: 00 UDC 541.7

Ch 3 ERÄMETSÄ, O: *On the Decomposition of Potash Felspar.* (Acta P 260/1959) 17 pp, Sw. Kr 7: 00 UDC 553.61:542.92

Ch 4 *Report of the Committee on Slaughtering Methods Appointed by the Danish Academy of Technical Sciences at the Request of the Ministry of Justice.* (Acta P 264/1959) 35 pp, Sw. Kr 7: 00 UDC 637.513.22

Ch 5 MÄKIPIRTTI, S: *On the Sintering of W-Ni-Cu Heavy Metal.* (Acta P 265/1959) 69 pp, Sw. Kr 7: 00 UDC 621.762:669.275.24.3

Ch 6 PAULSEN, A: *Constitution des Quatre Isomeres de Position des Chloro et Aminomethylbenzodioxannes-1,4, Substitues dans le Noyau Benzenique.* (Acta P 270/1960) 94 pp, Sw. Kr 7: 00 UDC 547.84:615.45

Ch 7 DAHLGREN, S-E: *Physico-Chemical Background of Phosphoric Acid Manufacture by Wet Processes.* (Acta P 271/1960) 15 pp, Sw. Kr 7: 00 UDC 661.634

Ch 8 SUNDIUS, N: *Felspar and its Influence on the Reactions in Ceramics during Burning.* (Acta P. 272/1960), 29 pp, Sw. Kr. 7: 00 UDC 666.6.041.9:553.61

Ch 9 DAHL, OLE: *Gamma Irradiation of Vacuum-Packed Sliced Meat Products.* (Acta P. 276/1960), 24 pp, Sw. Kr. 7: 00 UDC 664.91.037:539.166

Ch 10 ENEBO, LENNART AND PEHRSON, STIG O: *Thermophilic Digestion of a Mixture of Domestic Sewage Sludge and Cellulose Materials.* (Acta P. 281/1960) 40 pp, Sw. Kr. 7: 00 UDC 663.1:628.35:676.16

Ch 11 ASCHAN, L. J.: *Studies on the ternary system Cu-Mg-Si.* (Acta P. 285/1960) 46 pp, Sw. Kr. 7: 00 UDC 669.018.669.3.721.782 (084.2)

Ch 12 ERÄMETSÄ, OLAVI and KOLEHMAINEN, ANTTI: *A Modification of the Ion Characteristic to the Glass Theory and the Glasses Coloured with Lanthanons.* (Acta P. 290/1960). 22 pp. Sw. Kr. 7:00 UDC 666.24.01:546.65

Ch 13 ALERTSEN, AASE RYE: *Ageratochromene, a Heterocyclic Compound from the Essential Oil of Ageratum houstonianum Mill.* (Acta P. 293/1961). 66 pp. Sw. Kr. 7:00 UDC 547.81:547.913

Ch 14 SUNNER P, S. and WADSÖ, I: *Measurements of Heat Effects accompanying the wet Carbonization of Peat in the Temperature Range 20 to 220 Degrees C.* (Acta P. 297/1961). 40 pp Sw. Kr. 7:00 UDC 536.662:662.641

Price Sw. kr. 7:00

Printed in Norway
BJARNE H. REENSKAUG A.S

Library